SICOM & AOCO 2024

SOMS International Conference on Obesity & Metabolism

in conjunction with **Asia-Oceania Conference on Obesity**

Hosted by

SOMS Society for Korean Obesity and Metabolism Studies

Co-Hosted by

Asia Oceania Association for the Study of Obesity

aoaso

Sleep apnea in patient with obesity

Wonchul, SHIN

Neurology, KyungHee University

Hosp0italat Gangdong

SLEEP Dr. 신원철

꿀잠튜브

폐쇄성 수면무호흡증 _Obstructive Sleep Apnea: OSA
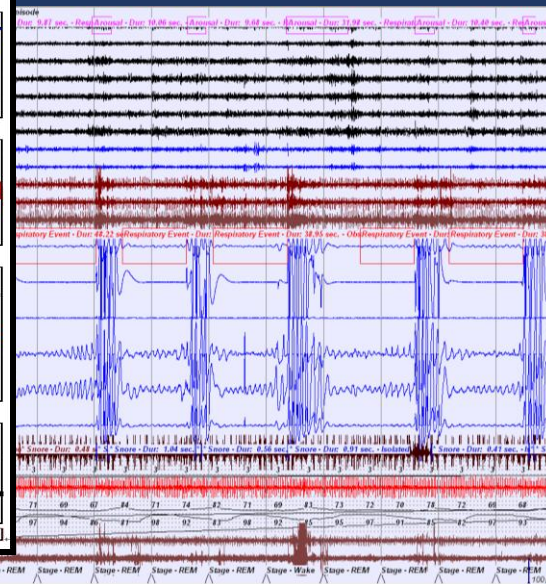
- **수면무호흡**
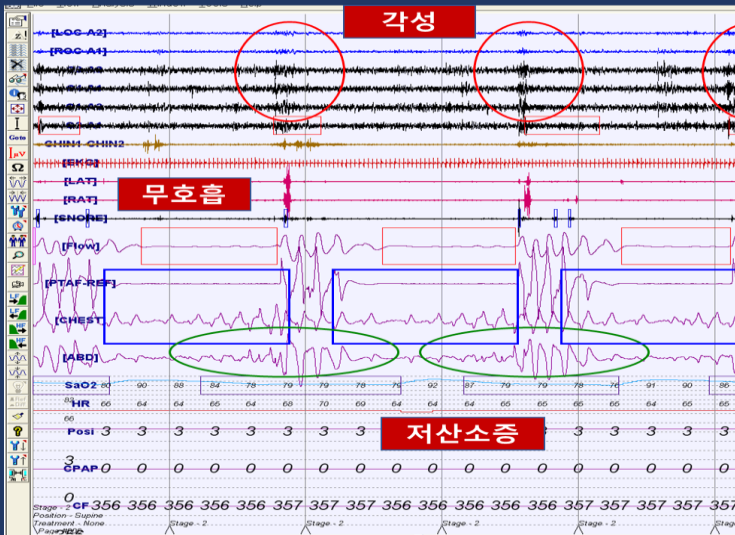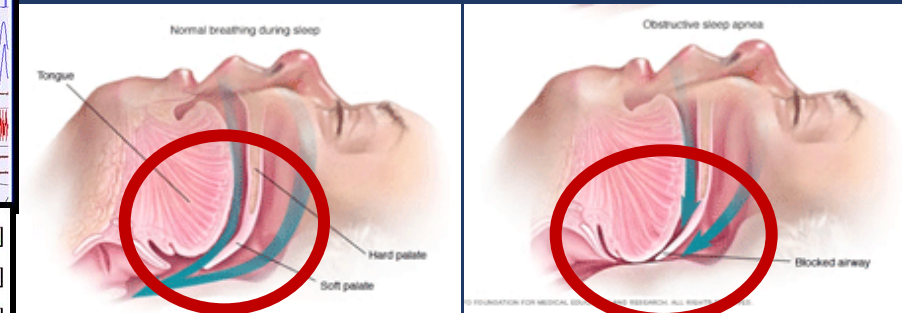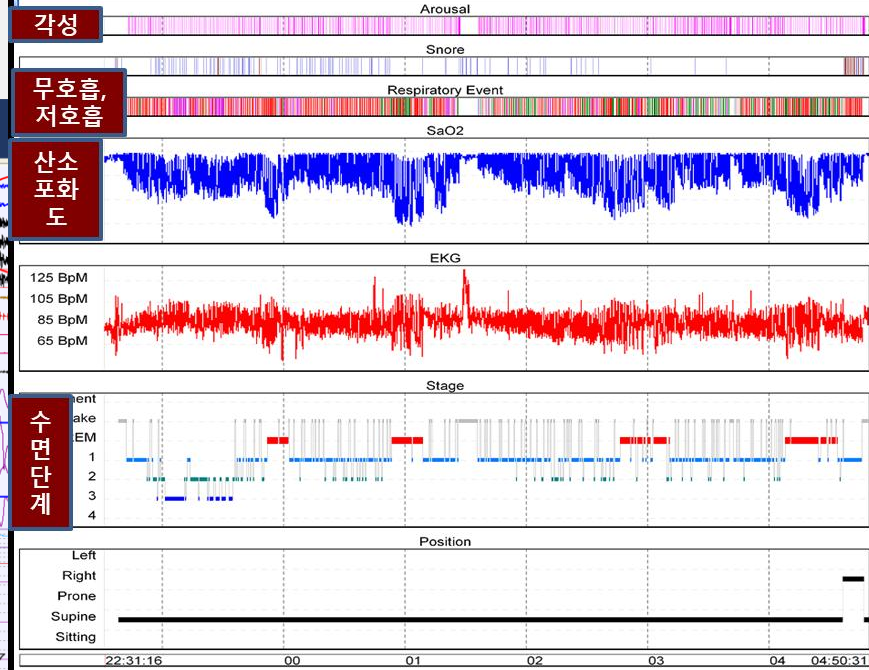
  수면 중 10초 이상 숨을 쉬지 않
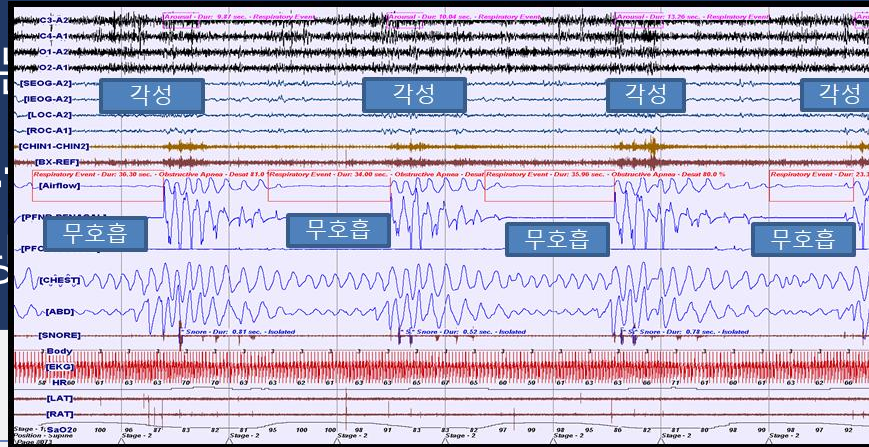
- **수면무호흡 - 저호흡 증후**

  잠자는 중, 수면무호흡이 시간당

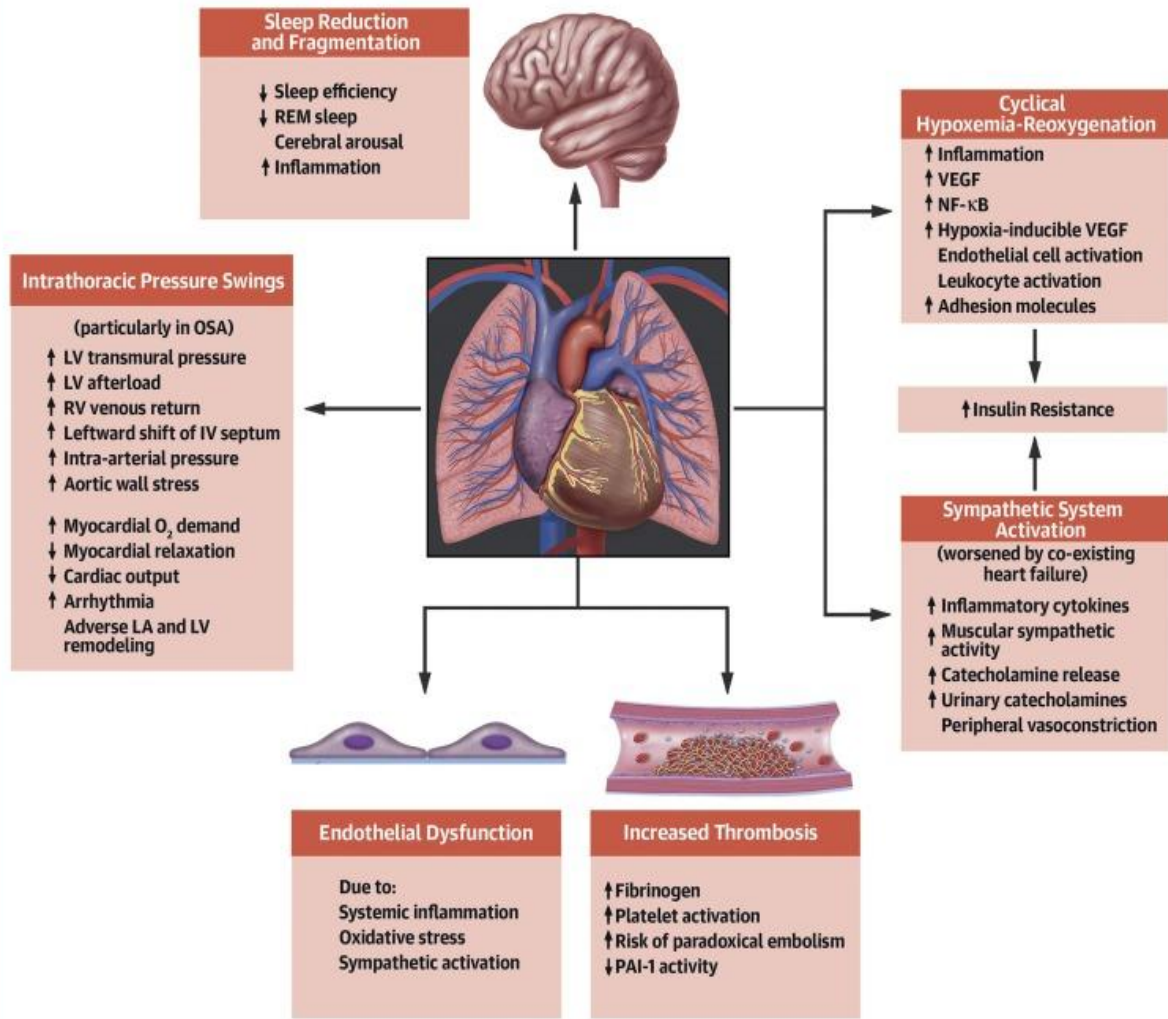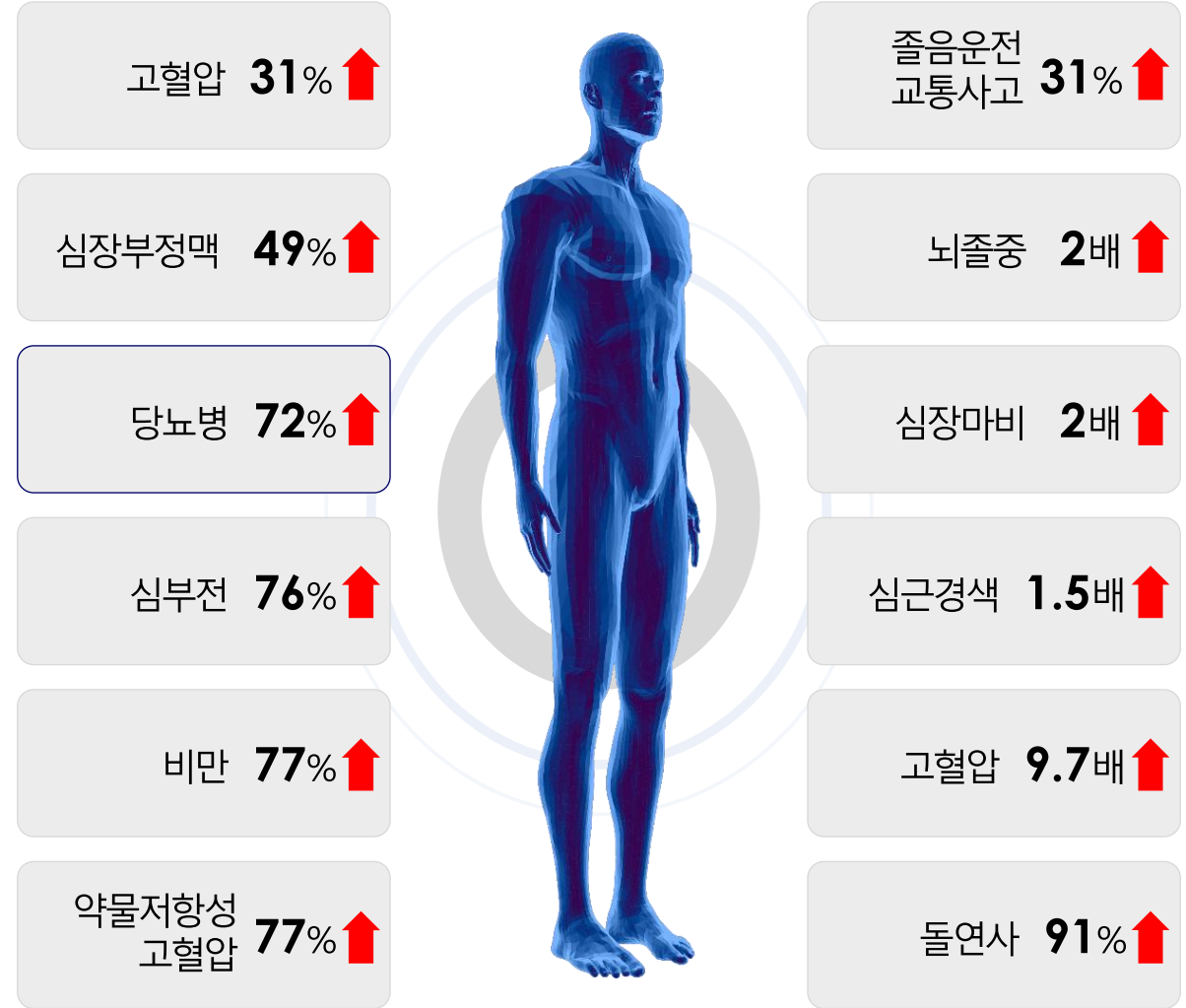| AHI 5	AHI 5 – 15
정상	경한 무호흡증

폐쇄성 수면무호흡증 _Obstructive Sleep Apnea: OSA

CENTRAL ILLUSTRATION: Pathophysiological Abnormalities in Sleep Disordered Breathing

Cowie, M.R. et al. J Am Coll Cardiol. 2021;78(6):608-624.

만성질환에 미치는 영향 및 합병증

- 고혈압 31%↑
- 심장부정맥 49%↑
- 당뇨병 72%↑
- 심부전 76%↑
- 비만 77%↑
- 약물저항성 고혈압 77%↑

- 졸음운전 교통사고 31%↑
- 뇌졸중 2배↑
- 심장마비 2배↑
- 심근경색 1.5배↑
- 고혈압 9.7배↑
- 돌연사 91%↑

Obstructive sleep apnea in patient with obesity
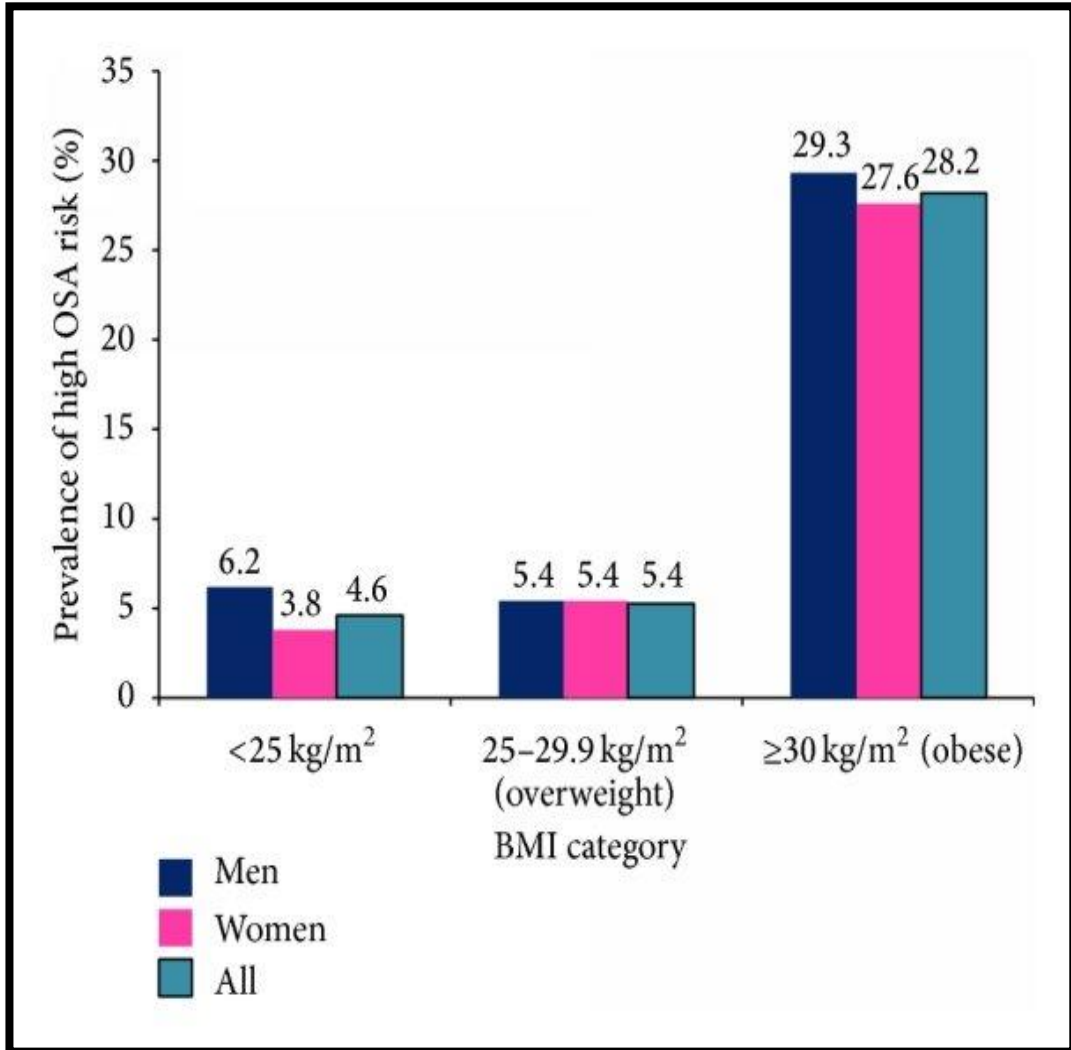
BMI	OSA Prevalence
25 kg/m^2 to 34.9 kg/m^2	33%
35 kg/m^2 to <40 kg/m^2	71%
40 kg/m^2 to <50 kg/m^2	74%
50 kg/m^2 to <60 kg/m^2	77%
≥60 kg/m^2	95%

Obstructive sleep apnea in patient with obesity

Six hundred ninety randomly selected employed Wisconsin residents ,4 years follow-up

A 10% weight gain predicted an ~32% increase in AHI and a 6-fold increase in the risk for developing moderate-to-severe sleep-disordered breathing
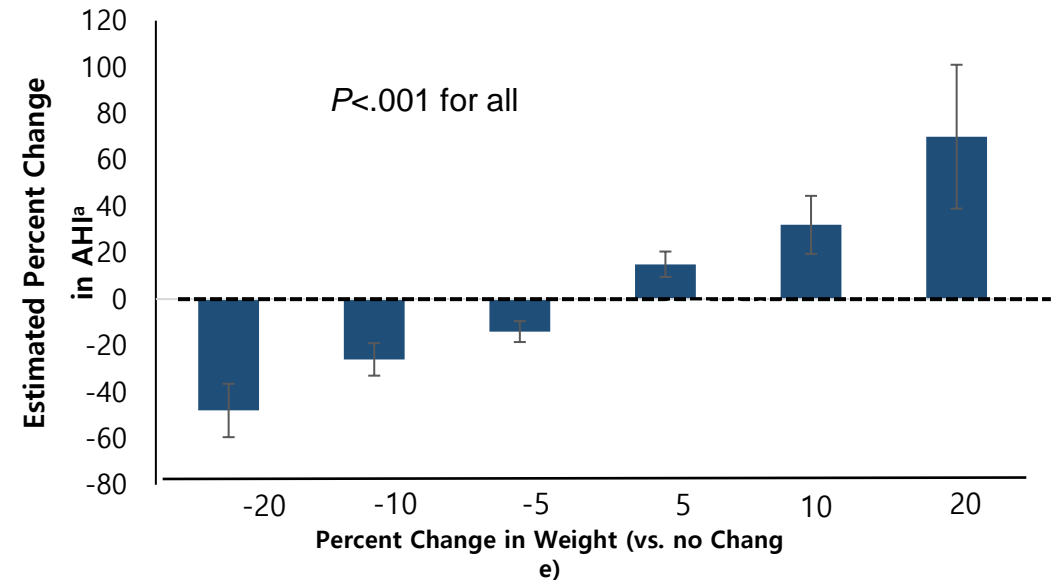
Table 1. Summary of Key Variables for Eligible Baseline Participants Invited for a Follow-up Study and Participants in the Follow-up Study*

Variable	Invited Participants Baseline (n = 948)	Follow-up Participants Baseline (n = 690)	Follow-up (n = 690)
Age, mean (SD), y	45 (8)	46 (7)	50 (7)
Male, No. (%)	542 (57)	385 (56)	385 (56)
AHI, events/hour			
Mean (SD)	4.5 (9.8)	4.1 (9.1)	5.5 (10.8)
Median	1.1	1.1	1.6
No. (%)			
<5	755 (80)	554 (80)	495 (72)
5-<15	120 (13)	90 (13)	127 (18)
≥15	73 (8)	46 (7)	68 (10)
Weight, mean (SD), kg	86 (20)	85 (19)	88 (20)
BMI, mean (SD), kg/m²	29 (6)	29 (6)	30 (7)
Neck girth, mean (SD), cm	38 (4)	38 (4)	38 (4)
Waist girth-to-hip girth ratio, mean (SD)	0.89 (0.09)	0.89 (0.09)	0.89 (0.09)
Skinfold total, mean (SD), mm†	80 (32)	81 (32)	106 (45)
Hypertensive, No. (%)‡	276 (29)	195 (28)	207 (30)
Smoker, No. (%)	181 (19)	120 (17)	112 (16)
Alcohol, mean (SD), drinks/wk	4 (7)	4 (7)	4 (5)

*AHI indicates apnea-hypopnea index; BMI, body mass index.
†Sum of biceps, triceps, subscapular, and suprailiac.
‡Blood pressure ≥140/90 mm Hg or current use of antihypertensive medications.

JAMA. 2000;284(23):3015-3021.

P<.001 for all

Estimated Percent Change in AHI[a] vs. Percent Change in Weight (vs. no Change)

Table 3. Conditional Logistic Regression Coefficients and Odds Ratios* for Development of Moderate-to-Severe Sleep-Disordered Breathing (SDB) (AHI≥15 Events/h) for Selected Increments of Weight Gain

| Percent Gain in Weight (vs No Gain)	Regression Coefficient (SE)	Estimated Odds Ratio for Moderate-to-Severe SDB (95% Confidence Interval)
5	0.9 (0.3)	2.5 (1.5 to 4.1)
10	1.8 (0.5)	6.0 (2.2 to 17.0)
20	3.6 (1.1)	36.6 (4.6 to >50)

*Adjusted for change in cigarette packs/wk. AHI indicates apnea-hypopnea index. All *P*<.001.
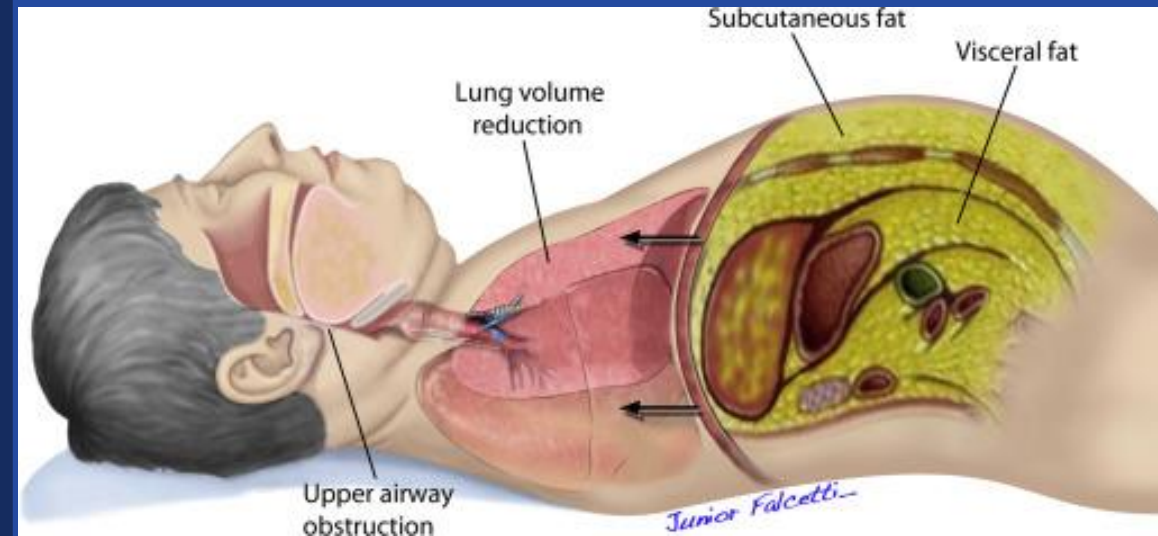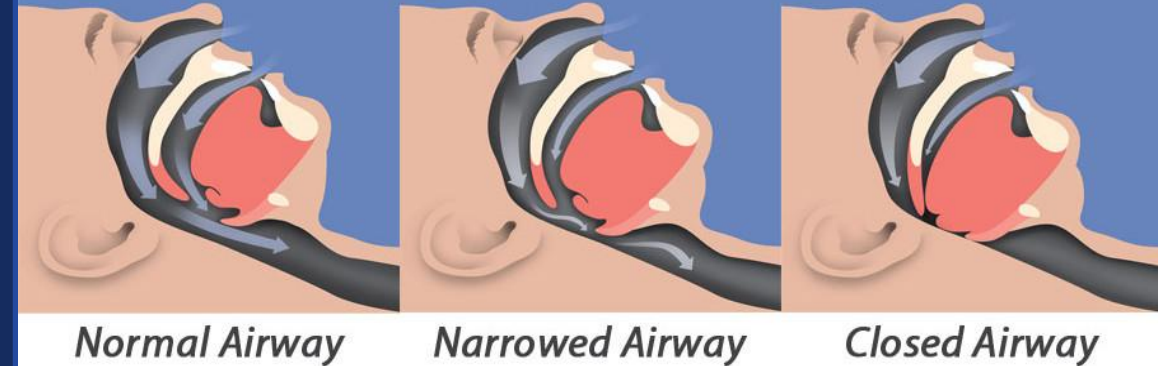
Obesity ➔ obstructive sleep apnea ; 위험 7배

폐쇄성수면무호흡증의 병리기전

1. 해부학적 문제 (High Critical closing pressure)
  - 비만, 편도, 작은턱

2. 상기도반사기능 소실 (low Upper airway reflex) ; 당뇨, 노화

3. 루프이득의 증가 (Elevated loop gain or unstable ventilatory control)

4. 낮은 뇌 각성 역치 (Low Arousal threshold)
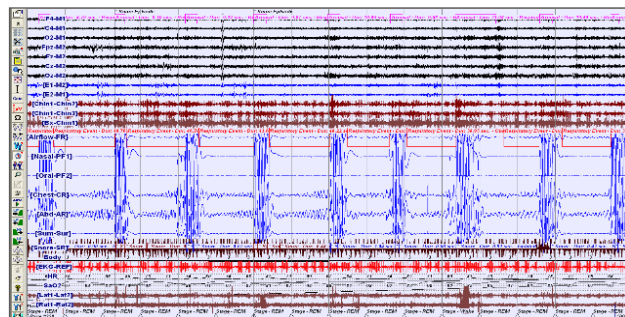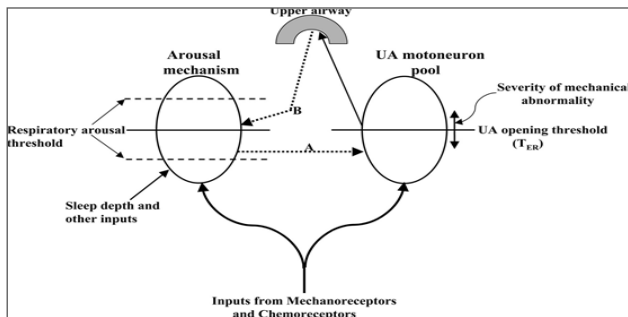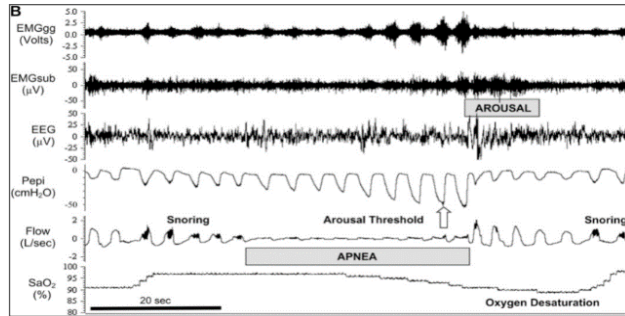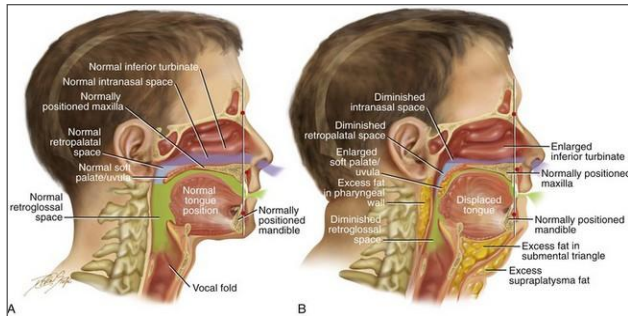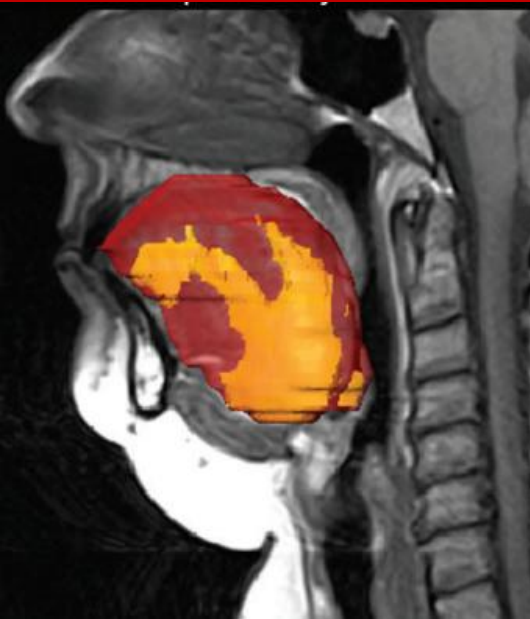
Obesity ➔ obstructive sleep apnea ; 위험 7배

Relationship Between Tongue Fat and OSA

Significant difference in tongue volume and tongue fat between patients with OSA and controls

Control		Apnea	
BMI	35 kg/m^2	BMI	34.2 kg/m^2
AHI	9.6 events/hr	AHI	59.1 events/hr
Tongue Volume	65,674 mm^3	Tongue Volume	95,492 mm^3
Tongue Fat Volume	16,056 mm^3	Tongue Fat Volume	41,686 mm^3
Tongue Fat Percentage	24%	Tongue Fat Percentage	42%

Average Tongue Volume

AHI=Apnoea-Hypopnoea Index; BMI=Body Mass Index; OSA=Obstructive Sleep Apnoea.
Data from Kim AM, et al. *Sleep*. 2014;37(10):1639-1648. Image is licensed under the NML Open Access Articles.

Changes in Tongue Fat Are Related to Weight Reduction and OSA

Association between percentage change in tongue fat with weight reduction or AHI change

Wang SH et al. *Am J Respir Crit Care Med*. 2020;201(6):718-727.
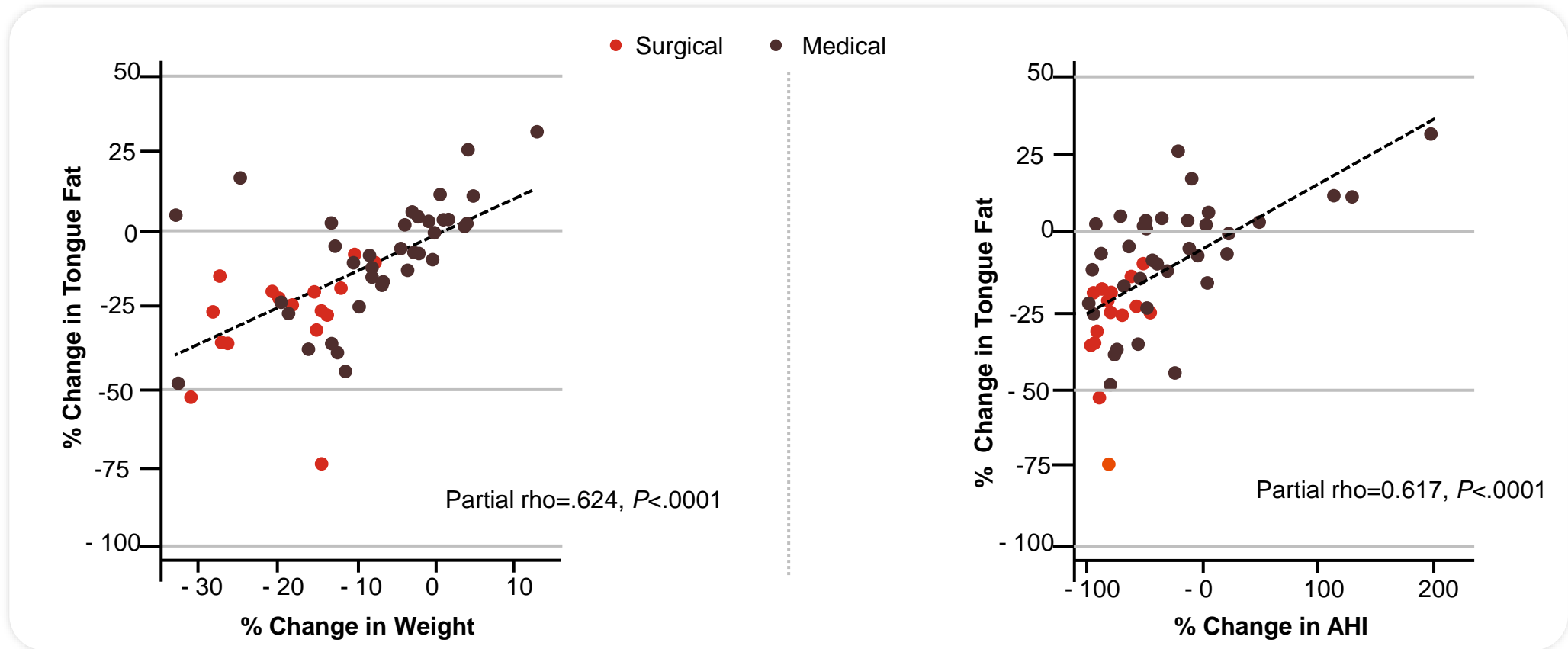
Obstructive sleep apnea in patient with obesity

AHI reduction
−11.7% in < 5%WLG , − 37.9% in 5%−10%WLG, and 49.3% in ≥ 10%WLG,

1-point drop in BMI (corresponding to 5–8 pounds, depending on a person's height, AHI decreases by 6.2%. And limiting BMI to 25–40 kg/m2 (which includes about 80% of the BMIs), then AHI drops by 7.1%.
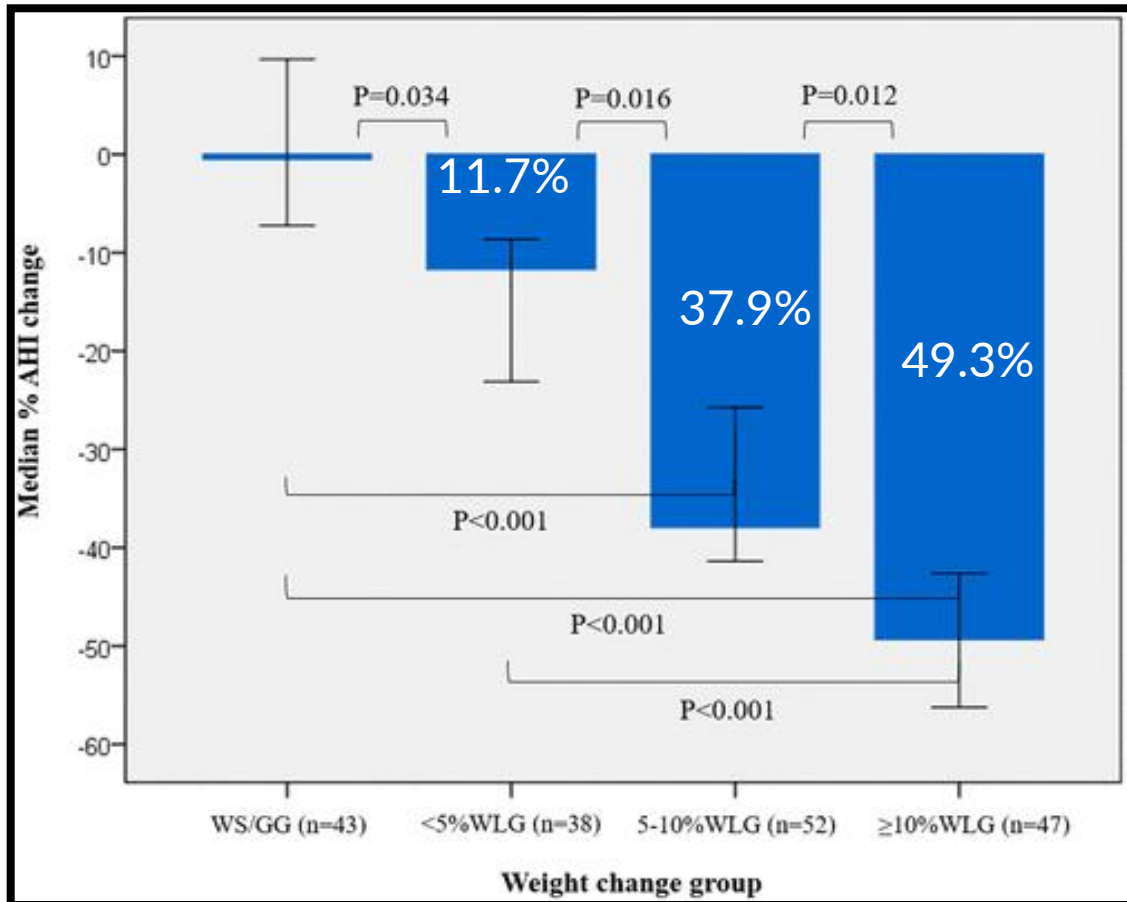
Clin Sleep Med. 2022;18(5):1251–1261.
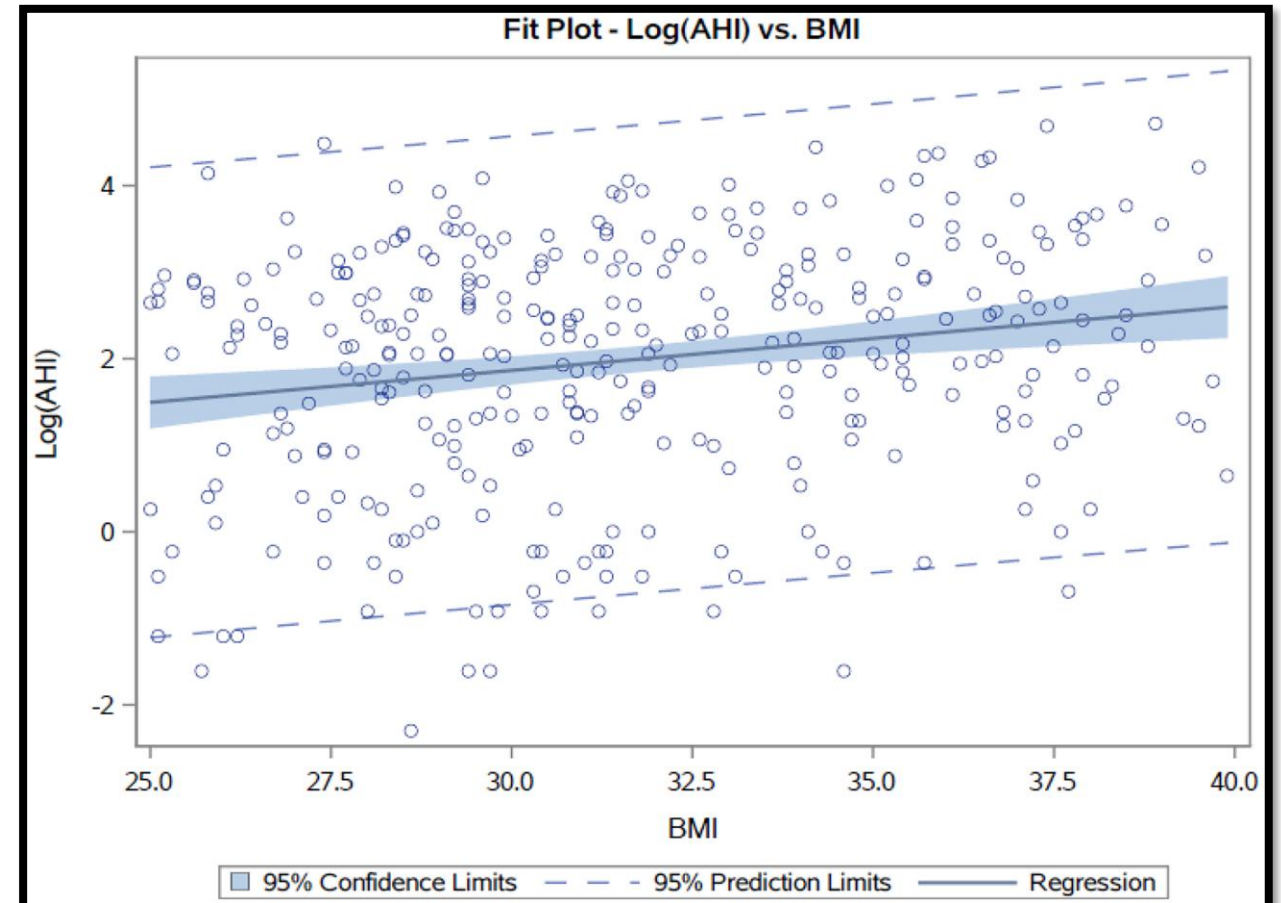
J Clin Sleep Med. 2022;18(12):2723–2729.

비만을 일으키는 원인들

유전

약물

활동 부족

수면부족

음식

스트레스

OSA ➔ Obesity

Obstructive sleep apnea

Sleep fragmentation

Intermittent Hypoxia

OSA ➔ Obesity

1. 호르몬 ; 렙틴 Vs 그렐린
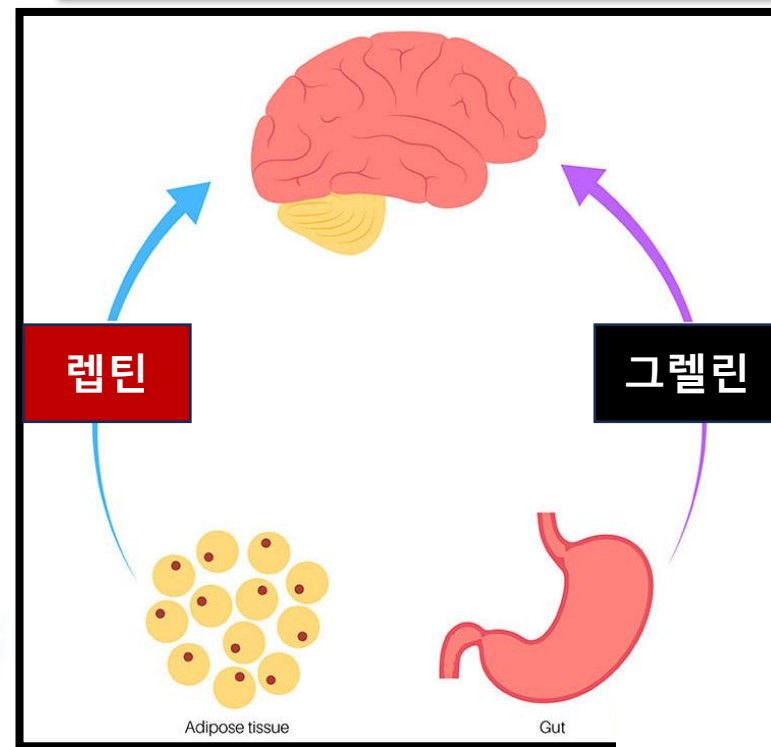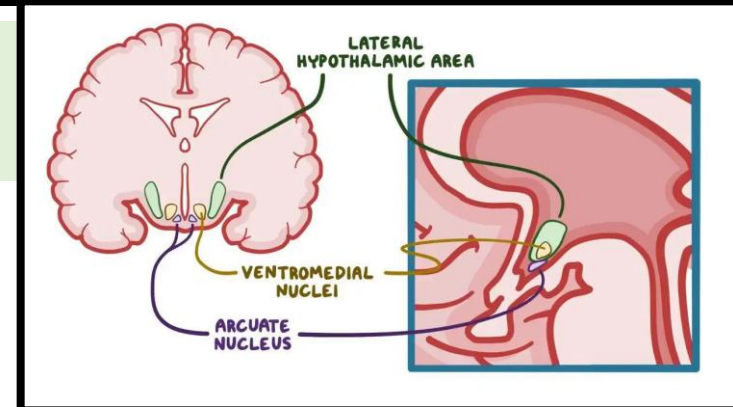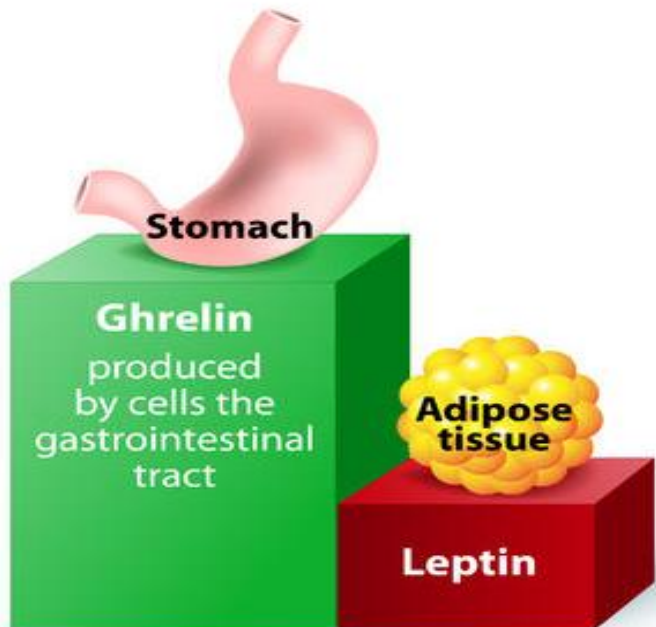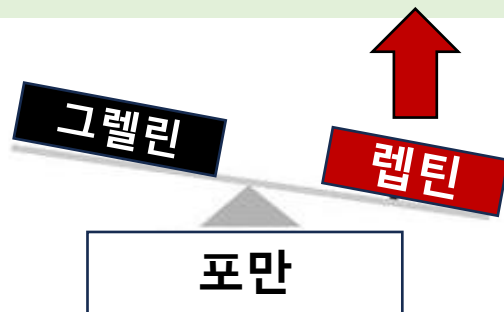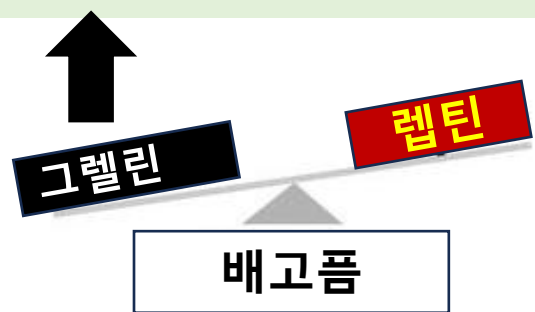
OSA ➜ Obesity

1. 호르몬 ; 렙틴 Vs 그렐린
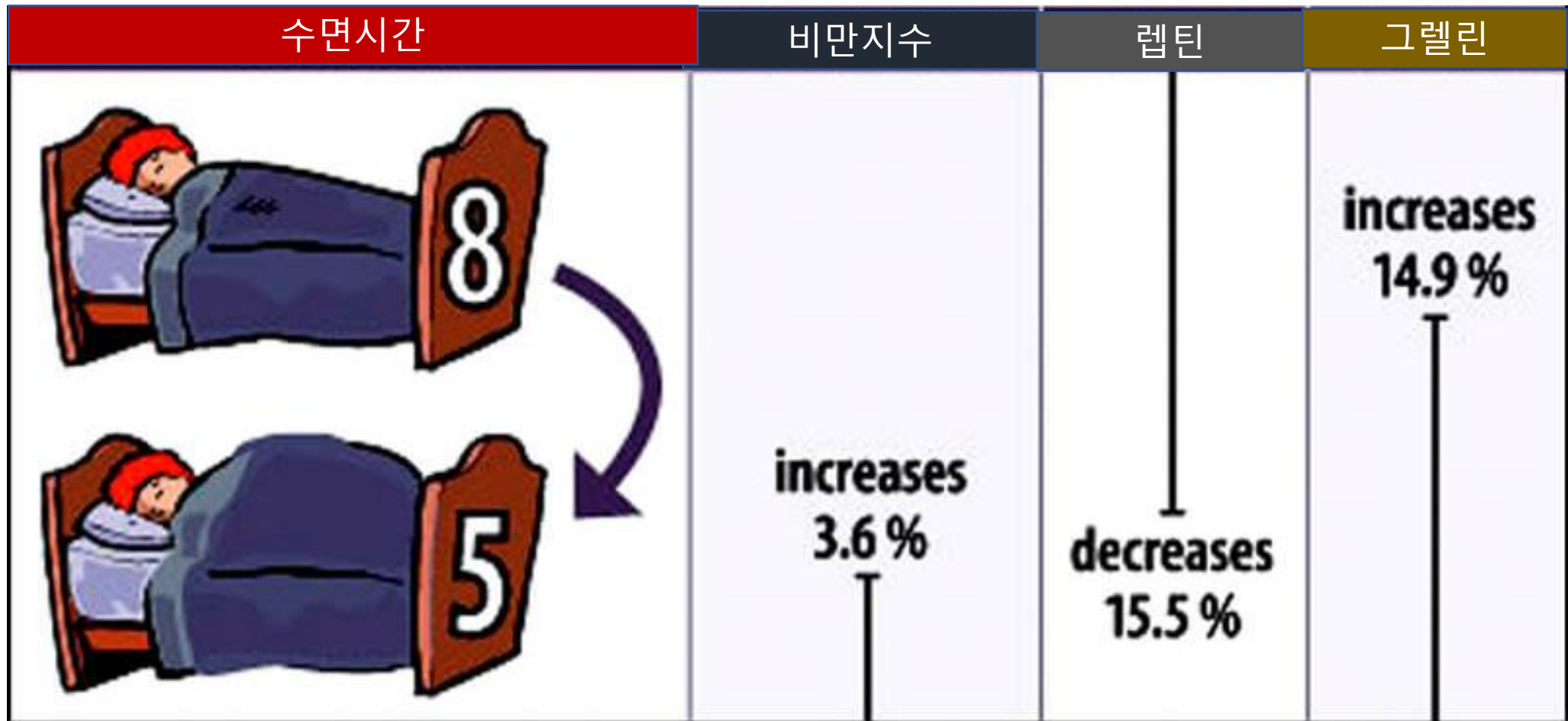
OSA ➔ Obesity

2. Cortisol, Growth Hormone
; 수면부족 ➔ 코티졸 증가, 성장호르몬 감소

성장호르몬

성장
호르몬
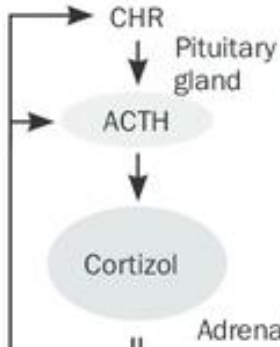
수면
부족

불안
우울

OSA ➔ Obesity

3. 대사장애
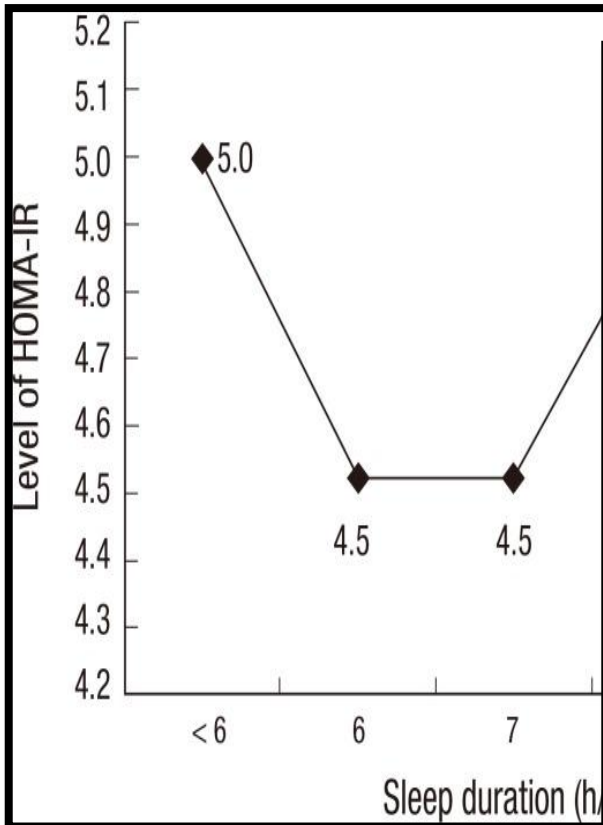
2013 Journal of Korean medical s

인슐린

수면시간

4. 활동력저하

정상 수면

수면부족

24 hours of sleep deprivation

Five nights of sleep restriction

근육 단백질
합성 변화 없음

근육 단백질
합성 저하

Sleep Medicine Reviews 2022
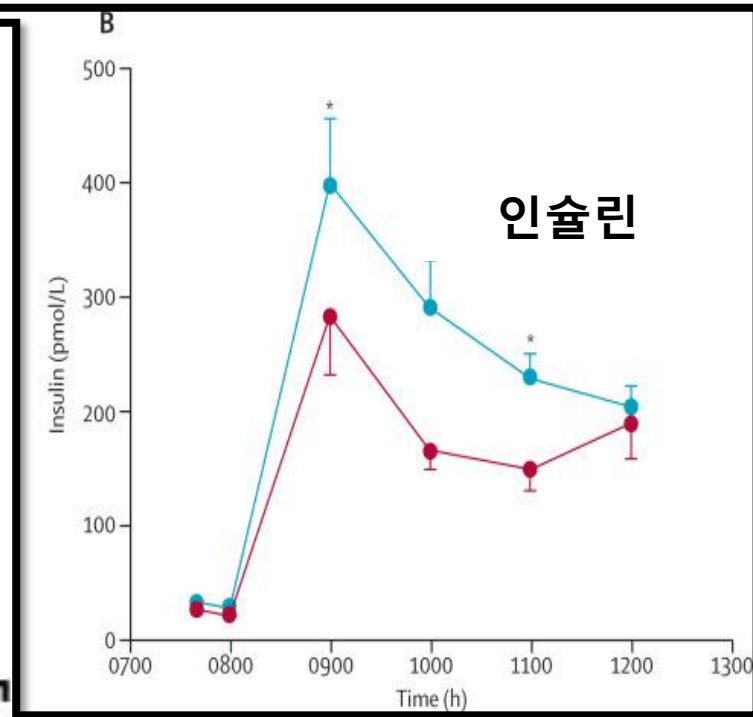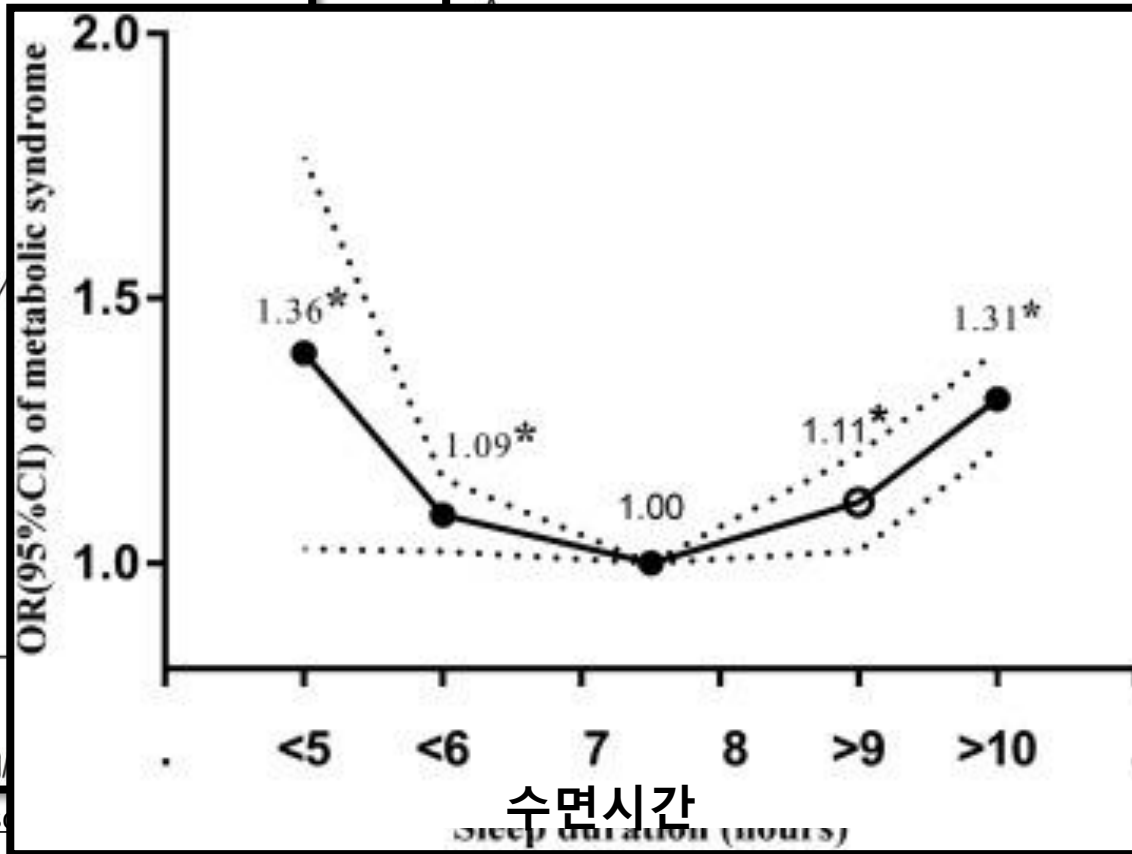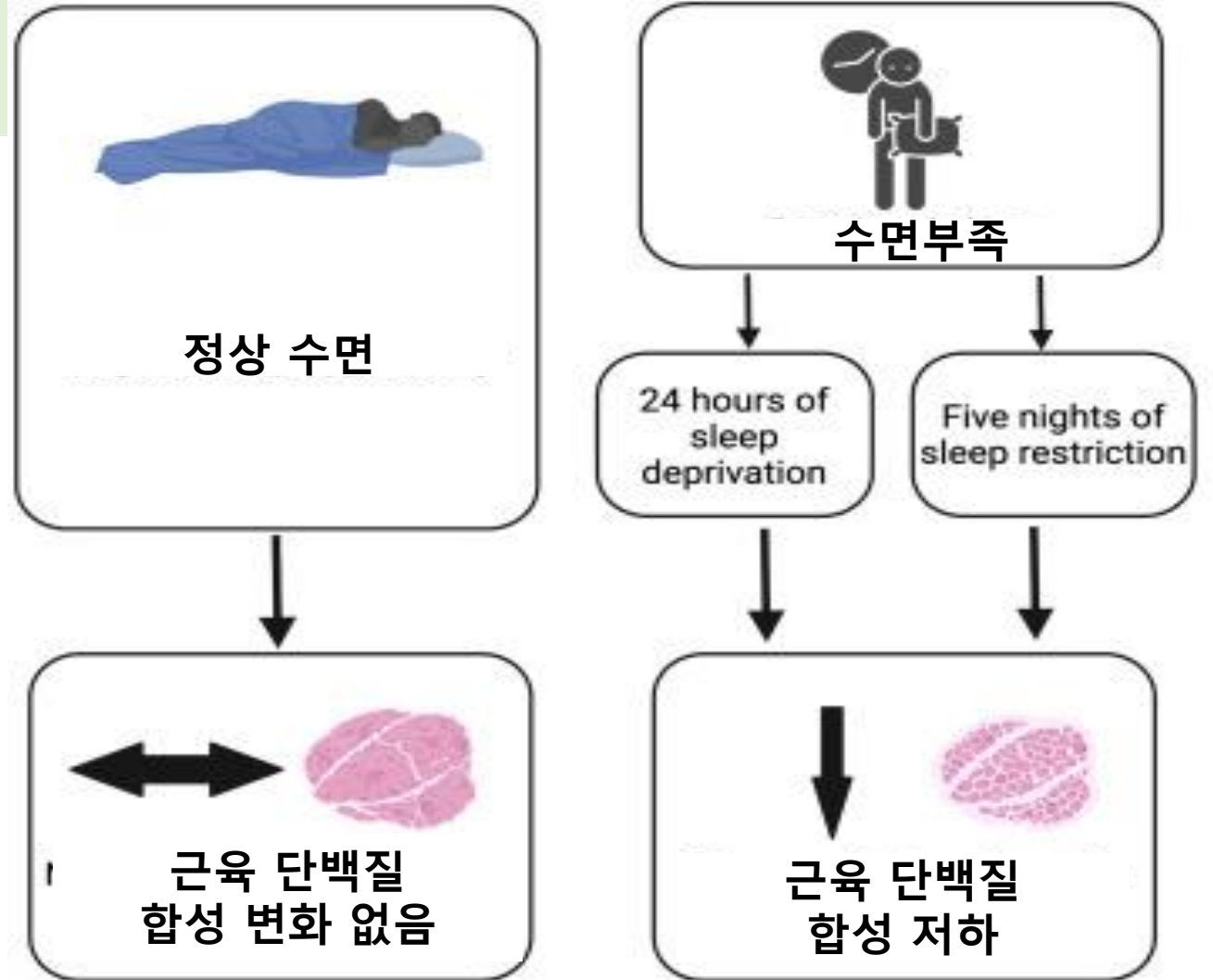
잠을 못자면...

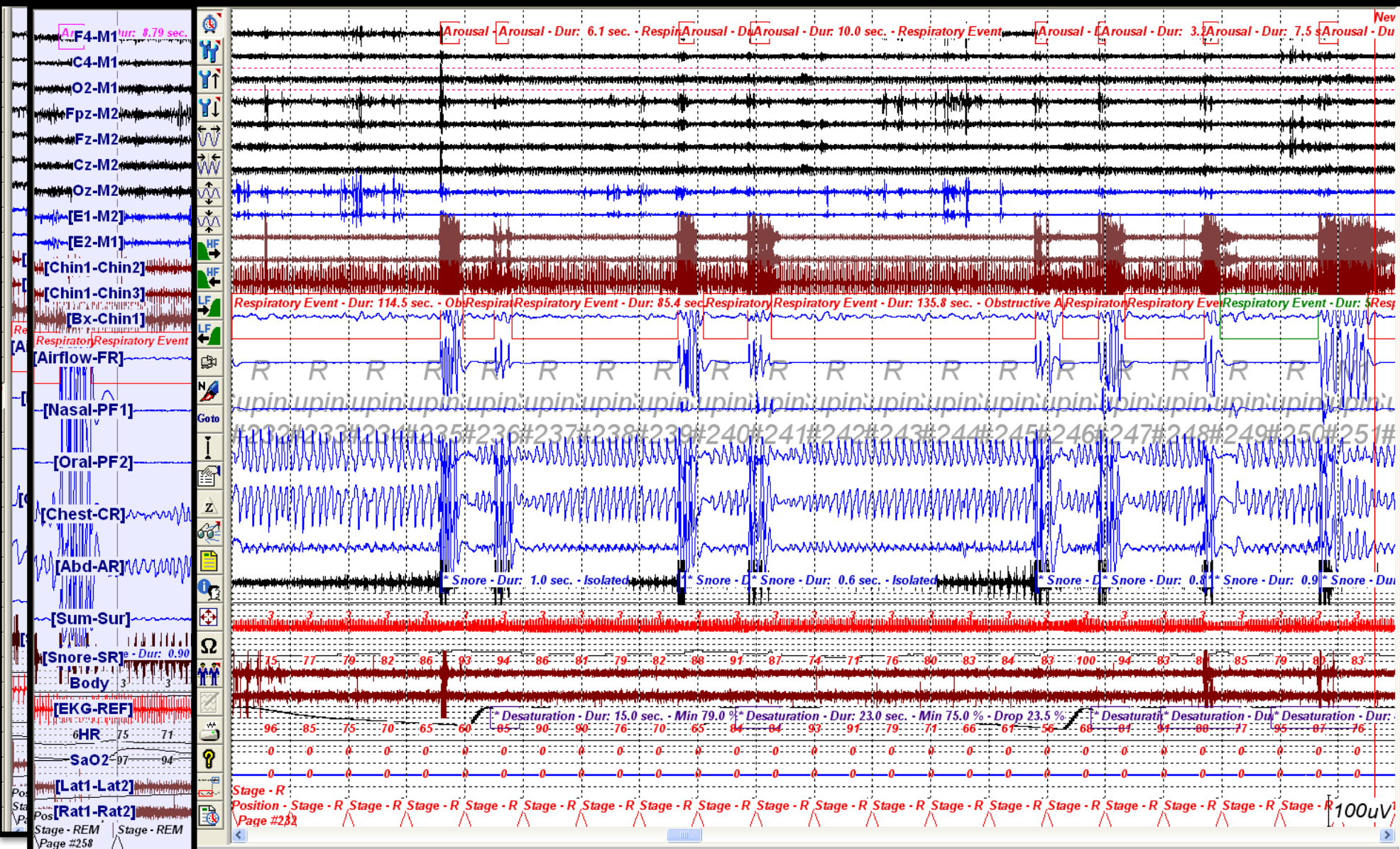| 🍗 배고픔	🔋 피로	⚛ 호르몬
과식	**활동 저하**	**에너지 대사 /이화작용**

| 체중 증가 | 근육감소 |

Obesity ⬅➡ obstructive sleep apnea
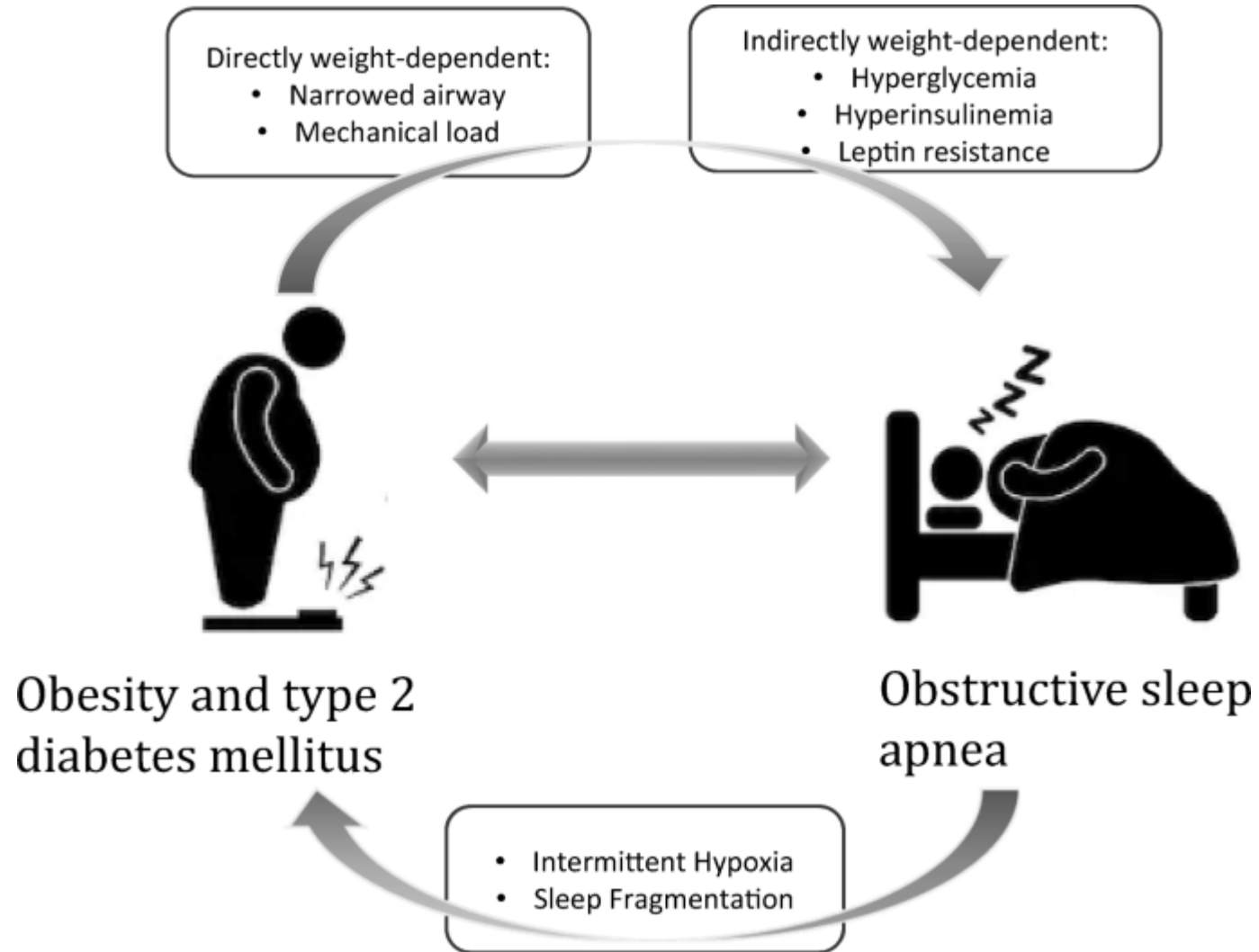
Treatment patient with obesity

- **운동하기**

- **충분하고, 질좋은 수면**
- **식사 조절 : 다이어트**

- **약물치료 ;** 제니칼, 큐시미아 ,
  삭센다, 위고비, 마혼자로

- **비만대사수술**
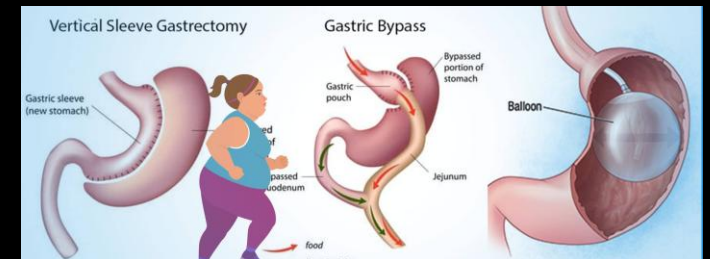
Treatment of Sleep apnea in patient with obesity

1 생활관리, 체중 감량

- 금주, 금연, 규칙적인 운동
- 옆으로 자는 훈련
- 정상 체중으로 감량하면, 수면무호흡증이
  20~30% 정도 호전됨. (AHI)
  - 운동, 식사
  - 약물치료
  - 비만대사수술

2 구강 장치 치료

- 맞춤형 마우스피스로 수면 중 턱을 앞으로
  당겨줌으로써 혀 뒤의 상기도 공간을 넓혀주어
  수면중 기도폐쇄를 막아 줌.
- 코골이, 경증의 수면무호흡증에 효과가 있으나
  중등도 이상의 수면무호흡증에는 효과가 제한됨.
- 보험급여가 안되어, 150-200만원의 고가의 비용

3 수술

- 침습적 치료법으로 부작용의 위험
- 구인두수술은 수면무호흡증에는
  효과가 없거나 미미함
- 양악전방이동 수술(MMA)는 고난이도의
  위험한 수술로, 비용이 매우 높음
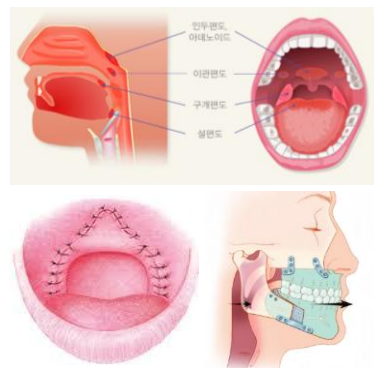
4 양압치료 (Positive Airway Therapy, PAP)

- **가장 효과적인 표준 치료법**
- 비침습적 치료법
- 수면 중 일정한 공기압력을 제공함으로써 기도가
  폐쇄 되는 것을 막아주는 줌.
- 고정형(CPAP), 자동형 양압기(APAP), 이중형 양압기(BiPAP)
- 착용의 불편감으로 인해서 착용율이 낮음 (50%)

수면무호흡증 환자에 대한 양압치료
Positive Airway Pressure therapy in OSA

Arousal

Snore

Respiratory Event

SaO2

100 %	
85 %	
70 %	
55 %	

PLM

EKG

125 BpM	
110 BpM	
95 BpM	
80 BpM	
65 BpM	

Stage

Movement	
Wake	
REM	
1	
2	
3	
4	

Position

Left	
Right	
Prone	
Supine	
Sitting	

22:58:22   00   01   02   03   04   05:19:43
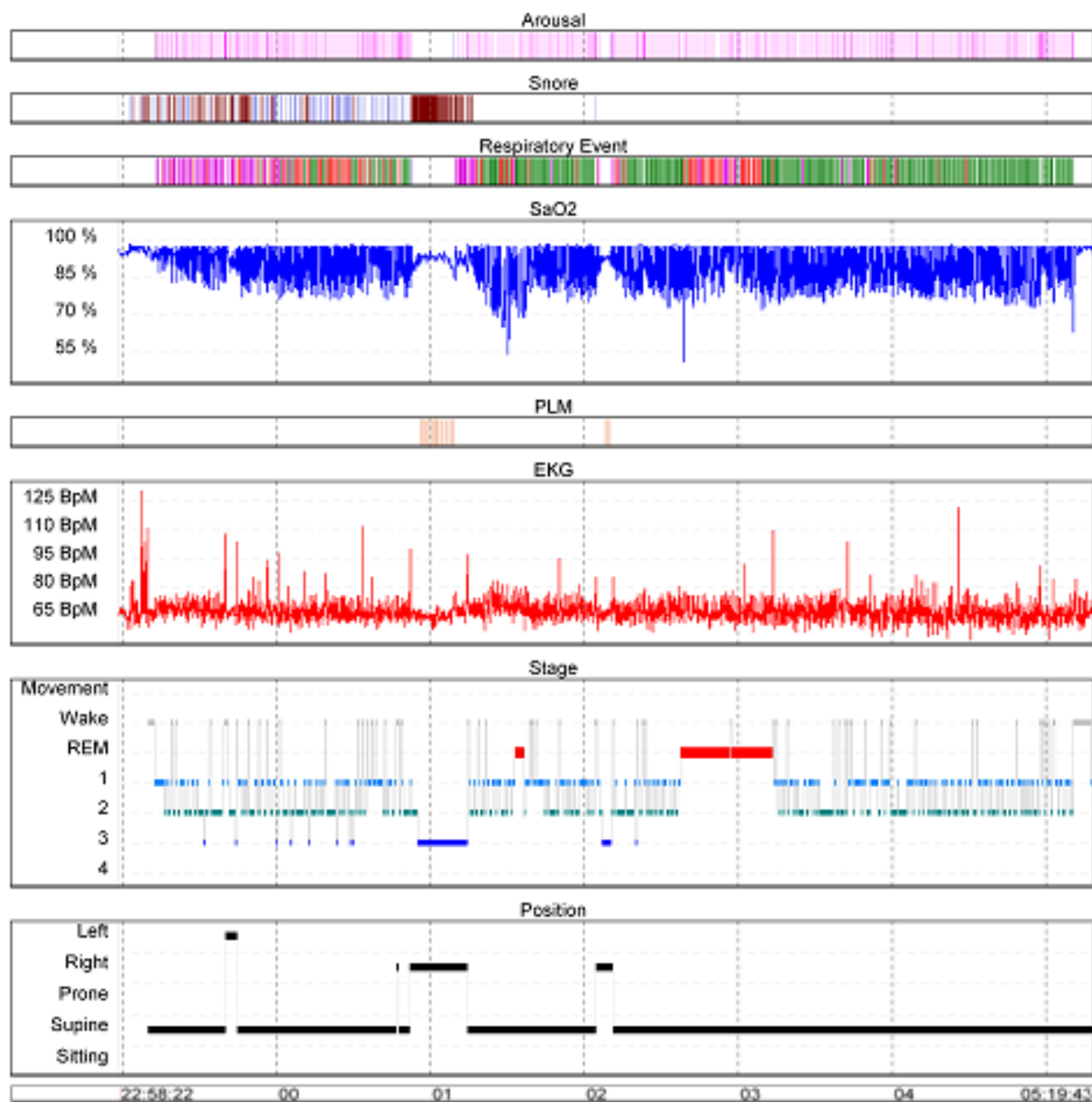
Optimal pressure →10.0cmH2)
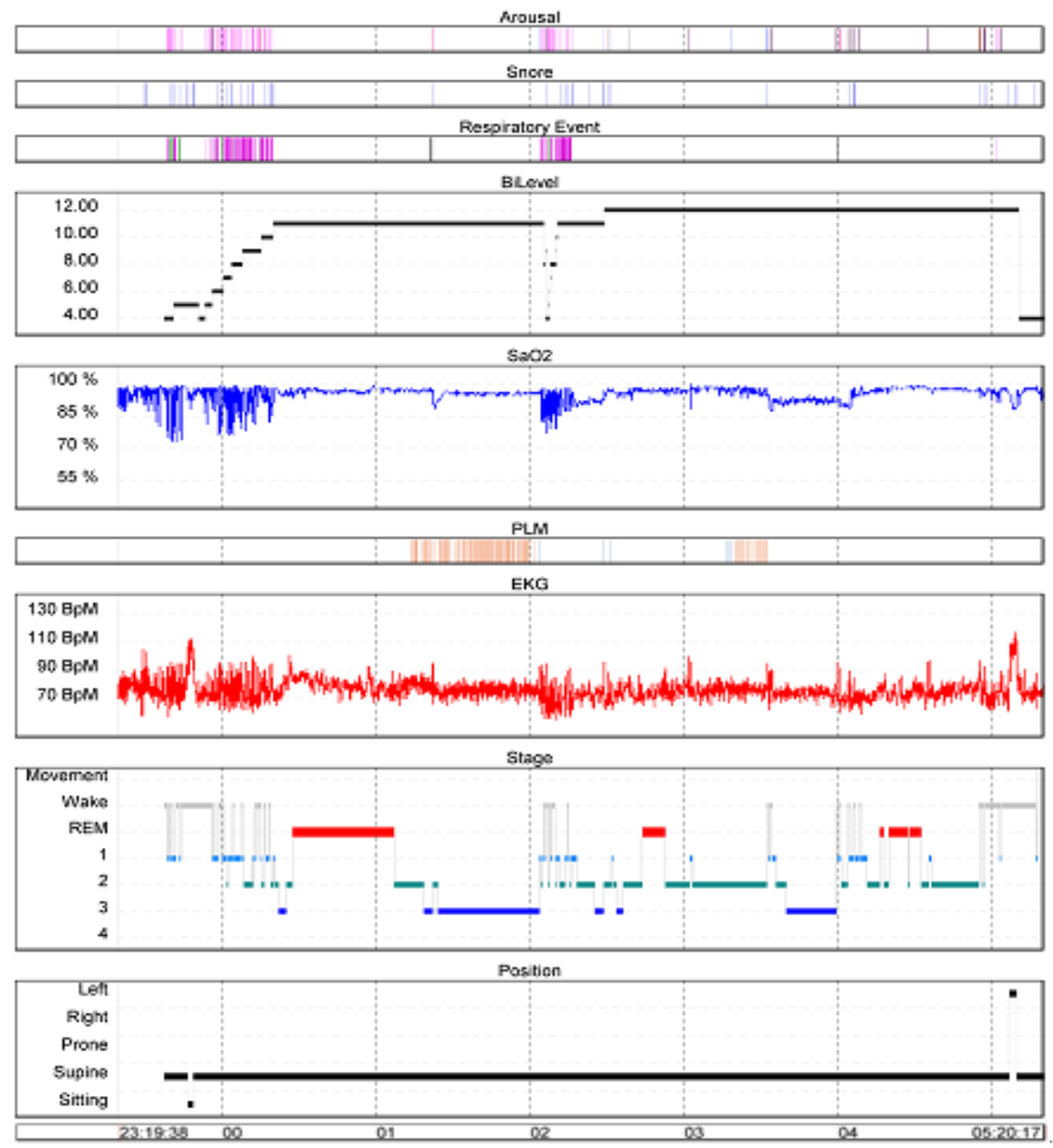
Improvement of Sleep apnea through weight reduction treatment

Weight Reduction With **Lifestyle Intervention** Was Associated with Improvements in OSA

Weight reduction from a low-energy diet improved OSA in men with obesity in a 9-week study

At Week 9, the intervention group's mean body weight was **19.8 kg** lower than that of the control group

Legend: Intervention (red) / Control (gray)
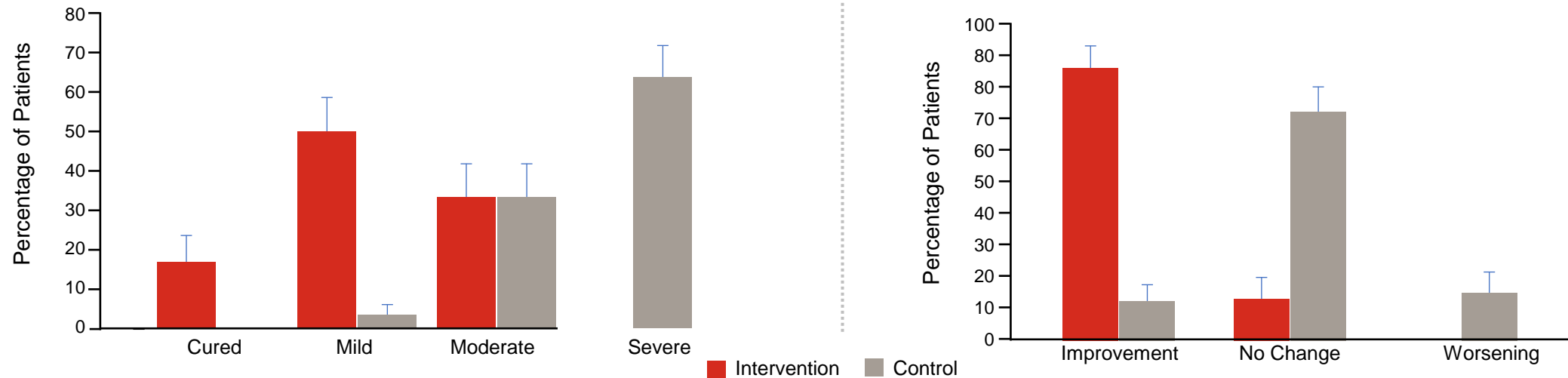
Note: Error bars indicate 95% confidence intervals

Definitions:
Cured: AHI <5 events/h; Mild: 5-14.9 events/h, Moderate: AHI 15-30 events/h; Severe >30 events/h.
Improvement in OSA: **Shift in severity of OSA** (i.e., moderate to cured or mild; or severe to cured, moderate or mild)
Worsening of OSA: opposite direction of improvement
No change in OSA: remaining within the same category of severity of OSA

Johansson K, et al. *BMJ*. 2009;339:b4609.

Greater Weight Reduction With **Anti-Obesity Medication** was Associated With Improved AHI

In both liraglutide and placebo groups, greater weight reduction was associated with greater reduction in AHI
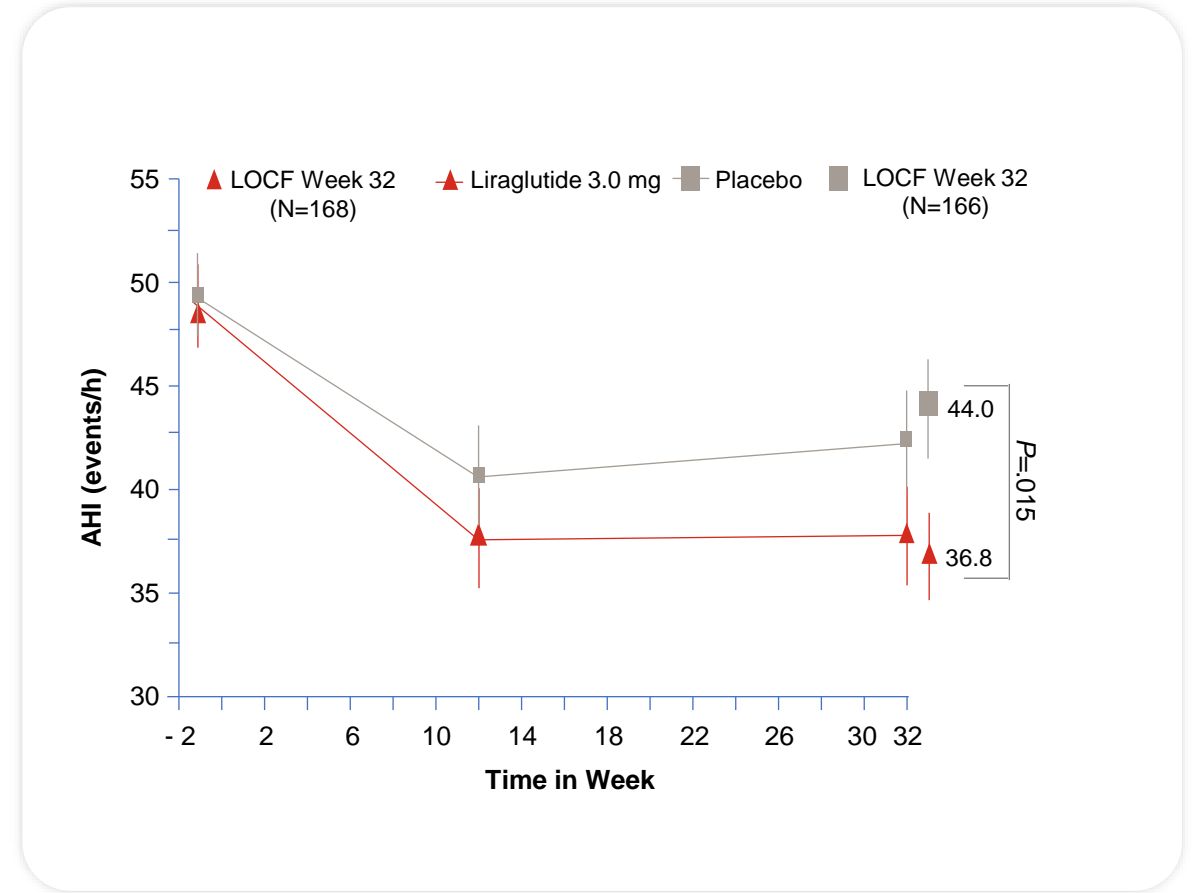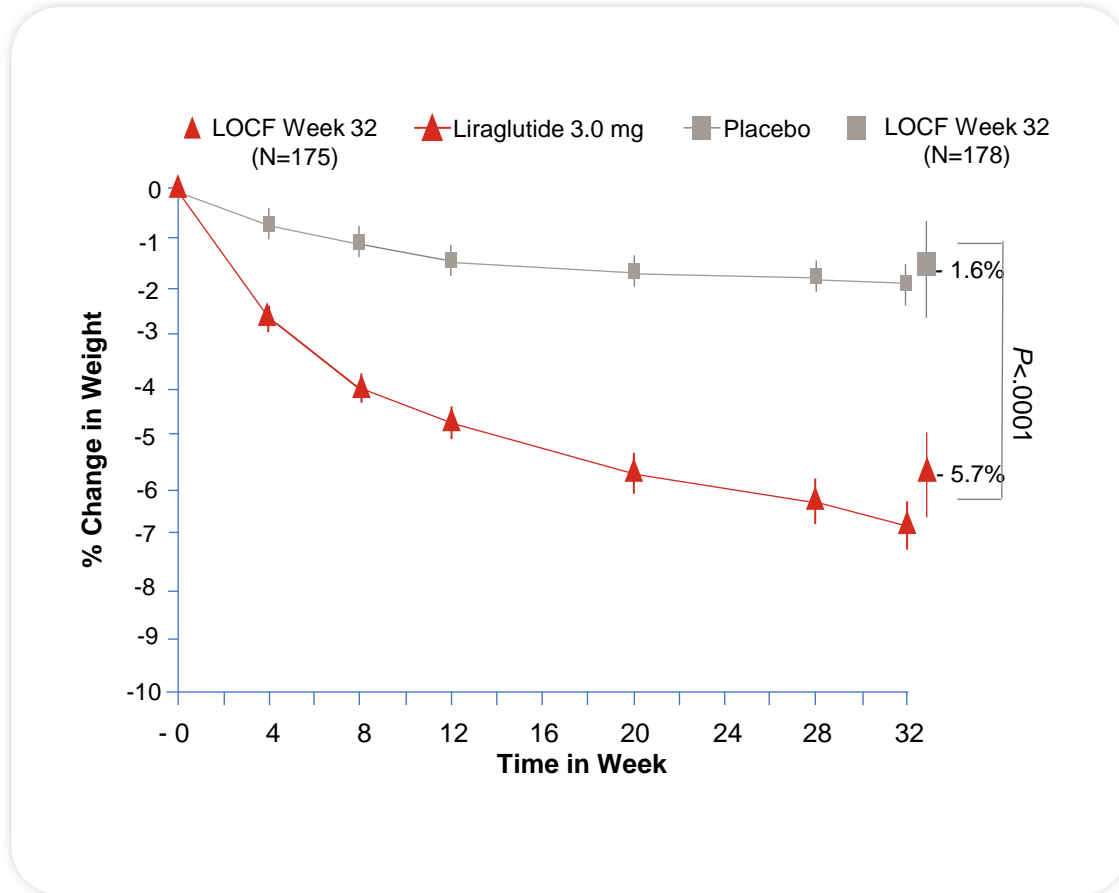
AHI=Apnoea-Hypopnoea Index; AOM=Anti-Obesity Medication; LOCF=Last Observation Carried Forward.
Blackman A, et al. *Int J Obes (lond)*. 2016;40(8):1310-9.

Improvements in AHI With Weight Reduction Associated With **Bariatric Surgery**

Weight reduction from bariatric surgery has shown a significant improvement in OSA

significant reduction in AHI (44.9 vs. 29.2), STOP-BANG (6.0 vs. 3.0), and ESS scores (12.0 vs. 5.0) (all p < 0.001) 12 months post-surgery.

Nastałek P, et al. *Sci Rep.* 2021;11(1):5003.
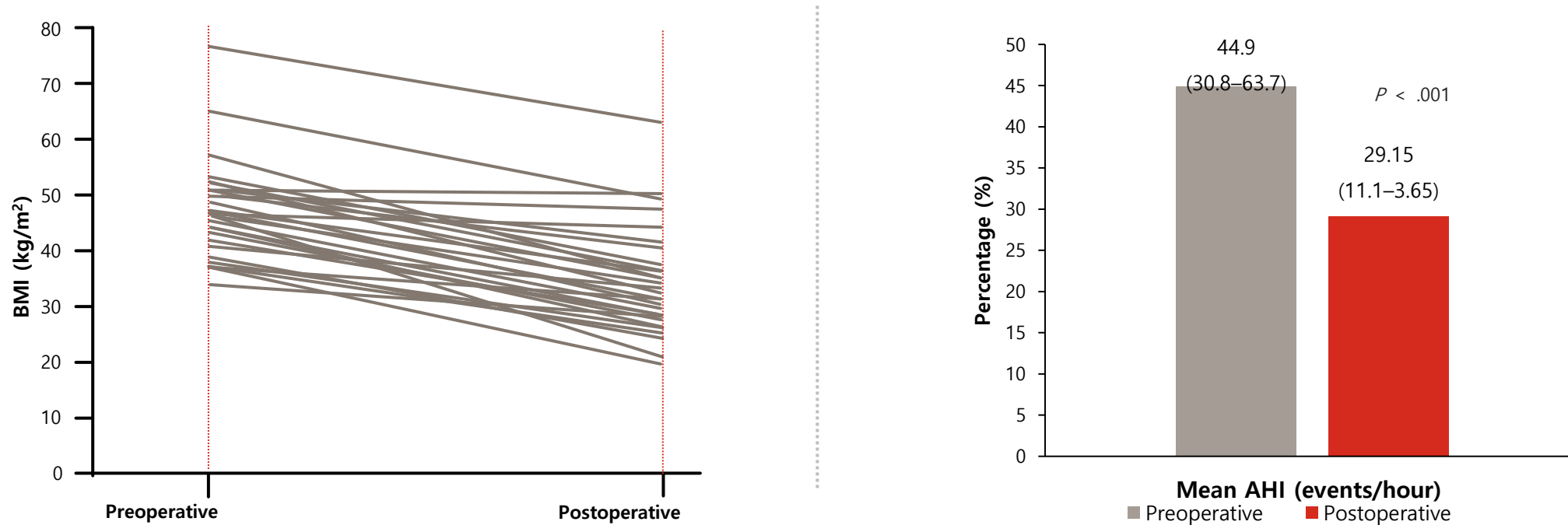
Results of a meta-analysis of 28 studies and 33 treatment arms
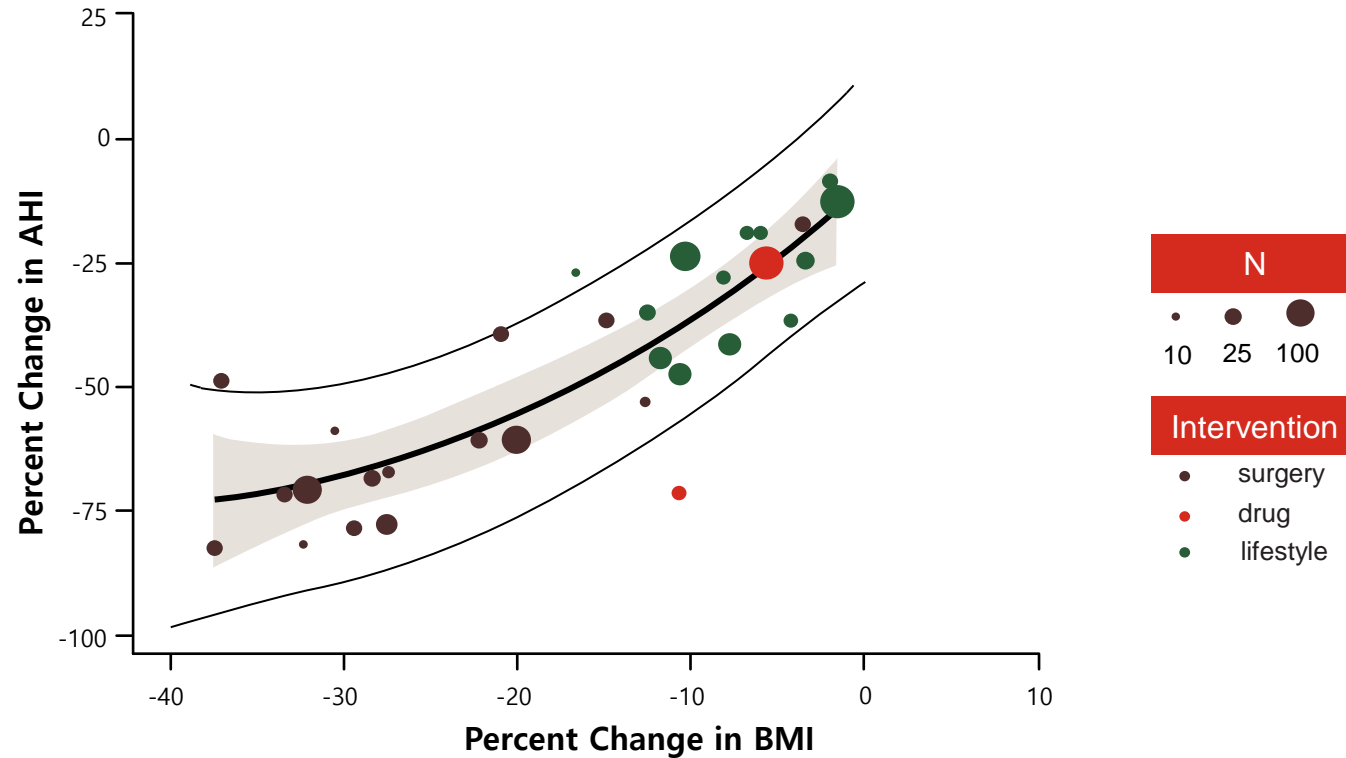
Based on the meta-regression, a BMI reduction of 20% was associated with AHI reduction of 57%. When BMI reduction exceeds 20%, the impact on sleep-disordered breathing was relatively smaller.
AHI=Apnoea-Hypopnoea Index; BMI=Body Mass Index; OSA=Obstructive Sleep Apnoea.
Malhotra A, et al. *Sleep Medicine*. https://doi.org/10.1016/j.sleep.2024.06.014. (Ahead of print).

Tirzepatide for OSA with obesity

SURMOUNT-OSA - Study

Phase 3, 52-week, randomised, double-blind, placebo-controlled master protocol to evaluate the efficacy and safety of TZP at the MTD (10 or 15 mg) vs. placebo as an adjunct to diet and exercise in participants with moderate-to-severe OSA (AHI ≥15 events/hour) and obesity (BMI ≥30 kg/m^2) without T2D[1-3]

Hypothesis:

TZP in people with OSA and obesity will yield important improvements in OSA severity as assessed by the AHI[1,2]

US, Australia, Brazil, China, Czechia, Germany, Japan, Mexico and Taiwan[3]

Study 1 (not on PAP)
2.5 mg | 5 mg | 7.5 mg | 10 mg | 12.5 mg | **TZP MTD QW (10 mg or 15 mg) (N=114)**

N=234

PBO QW (N=120)

Study 2 (on PAP)[a]
2.5 mg | 5 mg | 7.5 mg | 10 mg | 12.5 mg | **TZP MTD QW (10 mg or 15 mg) (N=120)**

N=235

PBO QW (N=115)

4 Weeks Screening

Adjunct to a reduced calorie diet and increased physical activity

Post-treatment Follow-up

Weeks → -4   0   4   8   12   16   20   24   36   48   52   +4

Dose Escalation | Maintenance Dose

Randomisation = 1:1

Primary outcome

[a]Participants in Study 2 were instructed to suspend PAP therapy for 7 days prior to PSG and PRO assessments at baseline, week 20, and week 52.

AHI=Apnoea-Hypopnoea Index; BMI=Body Mass Index; MTD=Maximum Tolerated Dose; OSA=Obstructive Sleep Apnoea; PAP=Positive Airway Pressure; PBO=Placebo; PRO=Patient Reported Outcomes; PSG=Polysomnography; QW=Once Weekly; R=Randomization; T2D=Type 2 Diabetes; TZP=Tirzepatide.

1. Malhotra A, et al. *Contemp Clin Trials.* 2024;141:107516. 2. https://clinicaltrials.gov/study/NCT05412004 (Accessed April 15, 2024). 3. Malhotra A, et al. *NEJM*. 2024;doi:10.1056/NEJMoa2404881 (Ahead of Print).

Key Inclusion and Exclusion Criteria of Participants

Adults ≥18 years of age

AHI ≥15 events/hour (CMS criteria)

BMI ≥30 kg/m^2

At least 1 self-reported unsuccessful dietary effort to lose BW

Key Inclusion Criteria[1,2]

Key Exclusion Criteria[1,2]

T1DM or T2DM and known obesity hypoventilation syndrome

Self-reported change in body weight >5 kg within 3 months before screening

Active device treatment of OSA other than PAP

Prior or planned surgical or endoscopic treatment for obesity, as well as surgery for sleep apnoea or major procedures related to ear, nose or throat

AHI=Apnoea-Hypopnoea Index; BMI=Body Mass Index; BW=Body Weight; CMS=Centers for Medicare and Medicaid Services; OSA=Obstructive Sleep Apnoea; PAP=Positive Airway Pressure; T1DM=Type 1 Diabetes Mellitus; T2DM=Type 2 Diabetes Mellitus.
1. Malhotra A, et al. *Contemp Clin Trials.* 2024;141:107516. 2. Malhotra A, et al. Poster presented at: *APSS 2023.* Poster: 171.

Baseline Characteristics
SURMOUNT-OSA Study 1: Participants Not on PAP Therapy

Parameters	Total (N=234)	TZP (N=114)	PBO (N=120)
Age (years)	47.9±11.5	47.3±11.0	48.4±11.9
<50 years	125 (53.4)	63 (55.3)	62 (51.7)
≥50 years	109 (46.6)	51 (44.7)	58 (48.3)
Female, n (%)	77 (32.9)	36 (31.6)	41 (34.2)
Race/ethnicity, n (%)			
Black or African American	13 (5.6)	6 (5.3)	7 (5.8)
American Indian or Alaska Native	18 (7.7)	9 (7.9)	9 (7.5)
Asian	47 (20.1)	23 (20.2)	24 (20.0)
White	154 (65.8)	74 (64.9)	80 (66.7)
Multiple	2 (0.9)	2 (1.8)	0
Hispanic or Latino	98 (41.9)	51 (44.7)	47 (39.2)
Body Weight, kg	114.7 ± 23.7	116.7 ± 24.6	112.8 ± 22.6
Mean BMI, kg/m^2	39.1 ± 7.0	39.7 ± 7.3	38.6 ± 6.7
BMI category, n (%)[a]			
<35	77 (32.9)	33 (28.9)	44 (36.7)
≥35 to <40	74 (31.6)	39 (34.2)	35 (29.2)
≥40	83 (35.5)	42 (36.8)	41 (34.2)
Waist circumference, cm	121.2 ± 15.7	122.6 ± 16.6	119.8 ± 14.8

Parameters	Total (N=234)	TZP (N=114)	PBO (N=120)
AHI, events/hour	51.5 ± 31.0	52.9 ± 30.5	50.1 ± 31.5
OSA severity[b], n (%)			
No Apnoea	1 (0.4)	0	1 (0.8)
Mild (≥5 to <15 AHI events/hour)	3 (1.3)	1 (0.9)	2 (1.7)
Moderate (≥15 to <30 AHI events/hour)	82 (35.2)	39 (34.2)	43 (36.1)
Severe (≥30 AHI events/hour)	147 (63.1)	74 (64.9)	73 (61.3)
Missing	1	0	1
ESS	10.6 ± 5.3	10.3 ± 5.3	10.8 ± 5.2
SASHB, %min/hour[c]	145.3 (103.4)	153.6 (102.7)	137.8 (104.1)
PROMIS Sleep-Related Impairment T-Score	53.8 ± 8.1	53.2 ± 7.5	54.3 ± 8.5
PROMIS Sleep Disturbance T-Score	53.6 ± 6.7	53.8 ± 6.0	53.5 ± 7.4
Hypertension, n (%)	177 (75.6)	84 (73.7)	93 (77.5)
Systolic BP (mmHg)	129.4 (11.5)	128.4 (12.2)	130.3 (10.7)
Diastolic BP (mmHg)	83.8 (8.7)	83.7 (8.9)	84.0 (8.6)
hsCRP (mg/L)	3.5 (122.0)	3.6 (124.6)	3.5 (120.0)
HbA1c (%)	5.67 ± 0.36	5.69 ± 0.37	5.64 ± 0.35
Prediabetes n (%)	152 (65.0)	74 (64.9)	78 (65.0)
Dyslipidemia n (%)	189 (80.8)	91 (79.8)	98 (81.7)

Note=Data are mean±standard deviation unless otherwise stated.
Footnotes, abbreviations and references are available in speaker notes section.
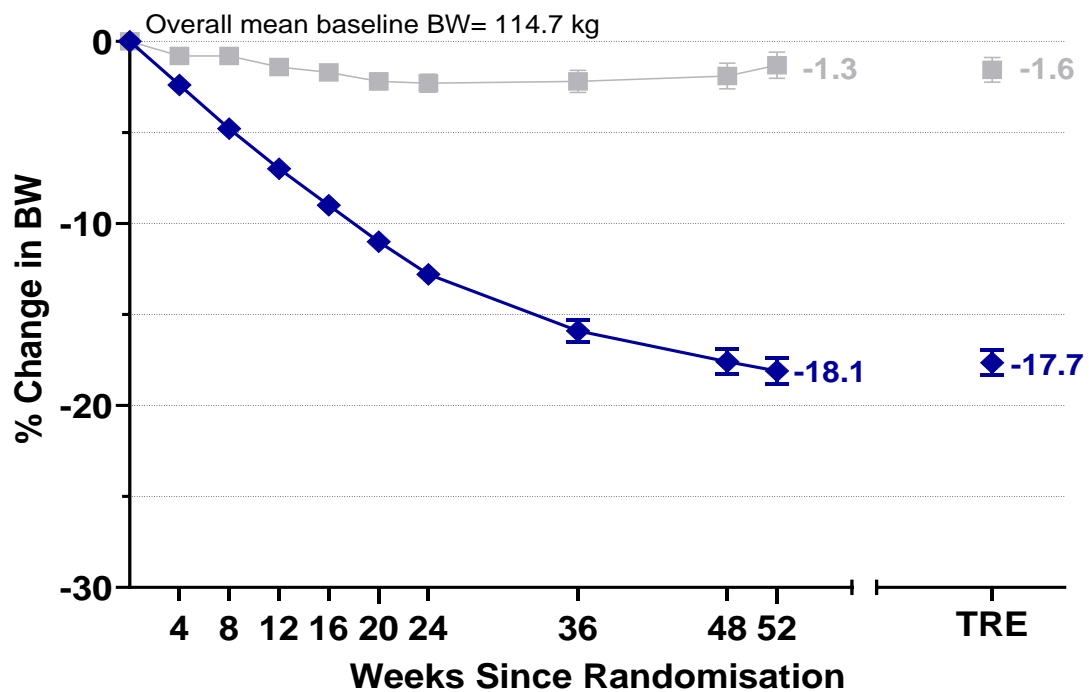
Percent Change in BW (TRE)

- -1.60 (-2.9 to -0.2)
- ETD -16.1 (-18.0 to -14.2) *P*<.001
- -17.7...

Percent Change in BW by Visit (Efficacy Estimand)

Overall mean baseline BW= 114.7 kg

- -1.3
- -1.6
- -18.1
- -17.7

Weeks Since Randomisation: 4 8 12 16 20 24 36 48 52 TRE

TZP[a] N=114   PBO N=120

Percent change in BW at Week 52 was a key secondary endpoint.

[a]TZP MTD is a maximum tolerated dose of 10 mg or 15 mg once weekly. The starting dose of 2.5 mg TZP was increased by 2.5 mg every 4 weeks until MTD was achieved. Participants who tolerated 15 mg continued on 15 mg as their MTD. Participants who tolerated 10 mg but did not tolerate15 mg continued on 10 mg as their MTD.

Note: Data are least-squares means (95% confidence interval) or n (%), unless otherwise stated. Changes are from baseline to Week 52.

BW=Body Weight; ETD=Estimated Treatment Difference; MTD=Maximum Tolerated Dose; PAP=Positive Airway Pressure; PBO=Placebo; TRE=Treatment-Regimen Estimand; TZP=Tirzepatide.

Malhotra A, et al. *NEJM*. 2024;doi:10.1056/NEJMoa2404881 (Ahead of Print).

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Change From Baseline in AHI at Week 52 (TRE)

Change in AHI by Visit (Efficacy Estimand)

TZP[a] N=114   PBO N=120

[a]TZP MTD is a maximum tolerated dose of 10 mg or 15 mg once weekly. The starting dose of 2.5 mg TZP was increased by 2.5 mg every 4 weeks until MTD was achieved. Participants who tolerated 15 mg continued on 15 mg as their MTD. Participants who tolerated 10 mg but did not tolerate 15 mg continued on 10 mg as their MTD.

Note: Data are least-squares means (95% confidence interval) or n (%), unless otherwise stated. Changes are from baseline to Week 52.

AHI=Apnoea-Hypopnoea Index; ETD=Estimated Treatment Difference; MTD=Maximum Tolerated Dose; PAP=Positive Airway Pressure; PBO=Placebo; TRE=Treatment-Regimen Estimand; TZP=Tirzepatide.
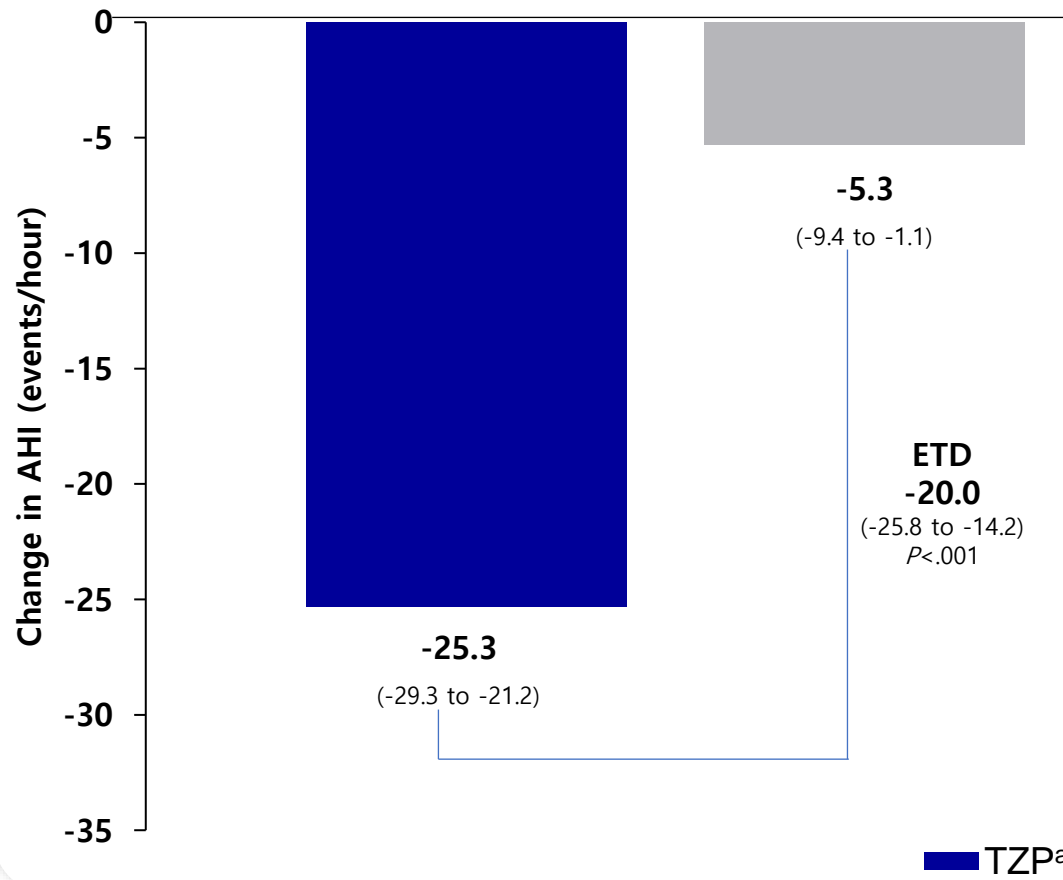
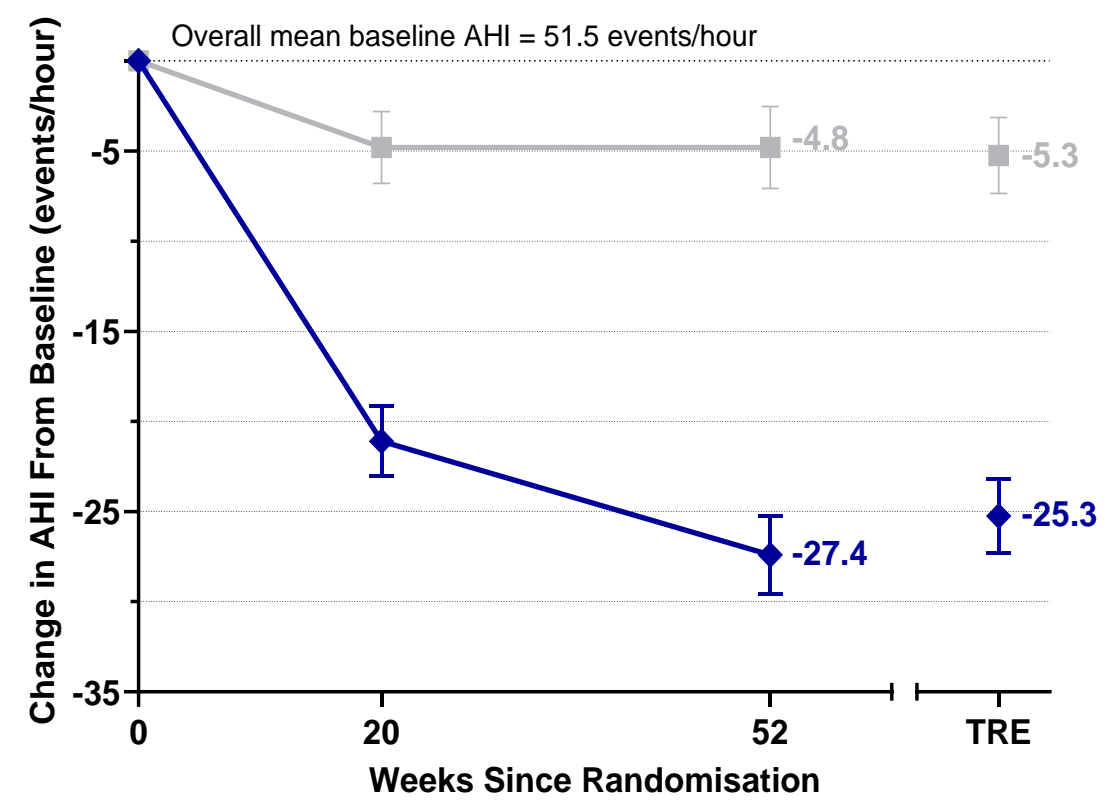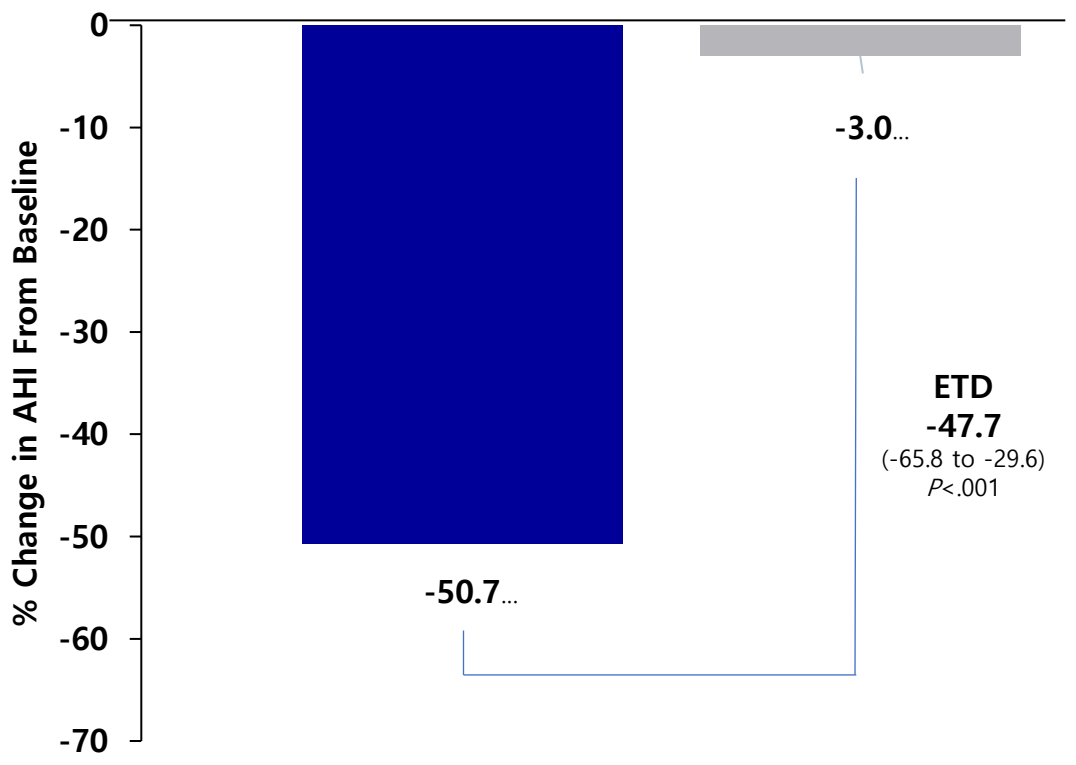Malhotra A, et al. *NEJM*. 2024;doi:10.1056/NEJMoa2404881 (Ahead of Print).   © 2024 Eli Lilly and Company

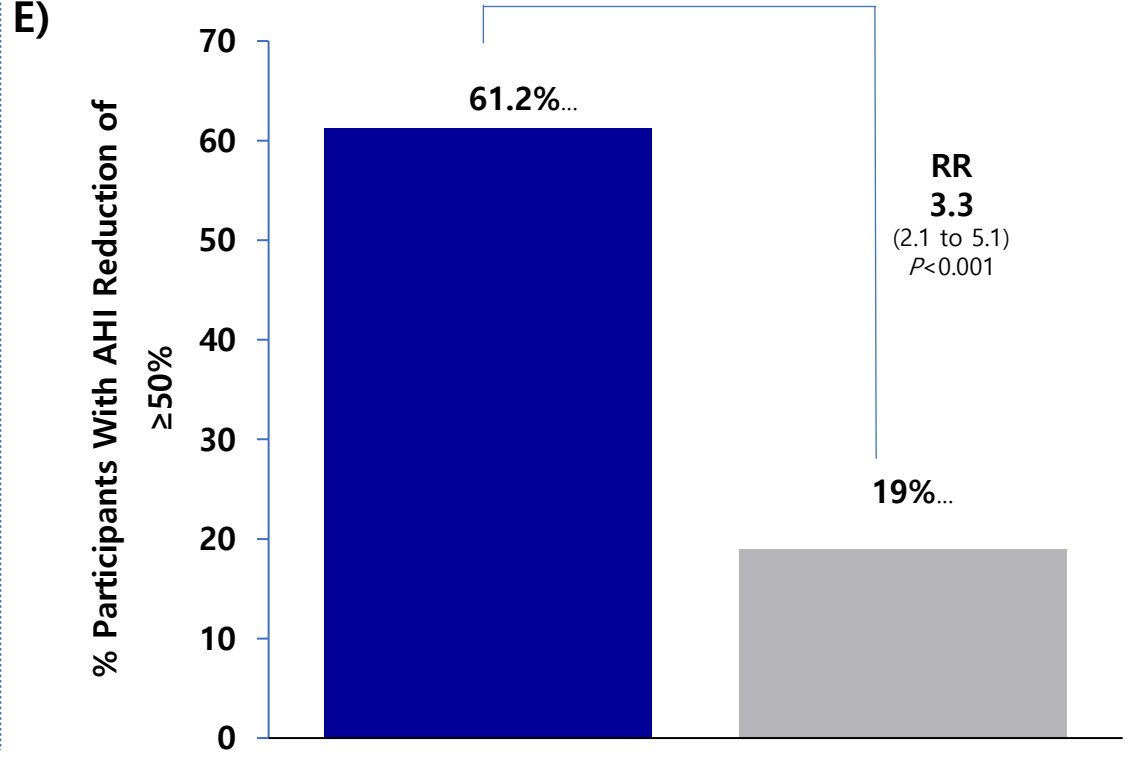# Change in Sleep Disordered Breathing-Related Endpoints
SURMOUNT-OSA Study 1: Participants Not on PAP Therapy

Percent Change From Baseline in AHI at Week 52 (TRE)

% Change in AHI From Baseline

- -3.0…
- ETD **-47.7** (-65.8 to -29.6) *P*<.001
- -50.7…

Participants With AHI Reduction of ≥50% at Week 52[a] (TRE)

% Participants With AHI Reduction of ≥50%

- 61.2%…
- RR **3.3** (2.1 to 5.1) *P*<0.001
- 19%…

■ TZP[b] N=114   ■ PBO N=120

Percent change in AHI at 52 weeks and participants with AHI reduction of ≥50% at 52 weeks were key secondary endpoints.

[a]Relative risks are calculated using g-computation methods from logistic regression. *P*-values for categorical endpoints are based on logistic regression model.

[b]TZP MTD is a maximum tolerated dose of 10 mg or 15 mg once weekly. The starting dose of 2.5 mg TZP was increased by 2.5 mg every 4 weeks until MTD was achieved. Participants who tolerated 15 mg continued on 15 mg as their MTD. Participants who tolerated 10 mg but did not tolerate15 mg continued on 10 mg as their MTD.

Note: Data are least-squares means (95% confidence interval) or n (%), unless otherwise stated. Changes are from baseline to Week 52.

AHI=Apnoea-Hypopnoea Index; ETD=Estimated Treatment Difference; MTD=Maximum Tolerated Dose; PAP=Positive Airway Pressure; PBO=Placebo; RR=Relative Risk; TRE=Treatment-Regimen Estimand; TZP=Tirzepatide.

Baseline Characteristics
SURMOUNT-OSA Study 2:

Parameters	Total (N=235)	TZP (N=120)	PBO (N=115)
Age (years)	51.7 ± 11.0	50.8 ± 10.7	52.7 ± 11.3
<50 years	99 (42.1)	54 (45.0)	45 (39.1)
≥50 years	136 (57.9)	66 (55.0)	70 (60.9)
Female, n (%)	65 (27.7)	33 (27.5)	32 (27.8)
Race/ethnicity, n (%)			
Black or African American	11 (4.7)	8 (6.7)	3 (2.6)
American Indian or Alaska Native	19 (8.1)	10 (8.3)	9 (7.9)
Asian	33 (14.1)	17 (14.2)	16 (14.0)
White	171 (73.1)	85 (70.8)	86 (75.4)
Multiple	-	-	-
Hispanic or Latino	98 (41.9)	51 (44.7)	47 (39.2)
Body Weight, kg	115.5 ± 22.0	115.8 ± 21.5	115.1 ± 22.7
Mean BMI[a], kg/m^2	38.7 ± 6.0	38.6 ± 6.1	38.7 ± 6.0
BMI category, n (%)[a]			
<35	66 (28.3)	33 (27.7)	33 (28.9)
≥35 to <40	88 (37.8)	47 (39.5)	41 (36.0)
≥40	79 (33.9)	39 (32.8)	40 (35.1)
Waist circumference, cm	121.2 ± 15.7	122.6 ± 16.6	119.8 ± 14.8

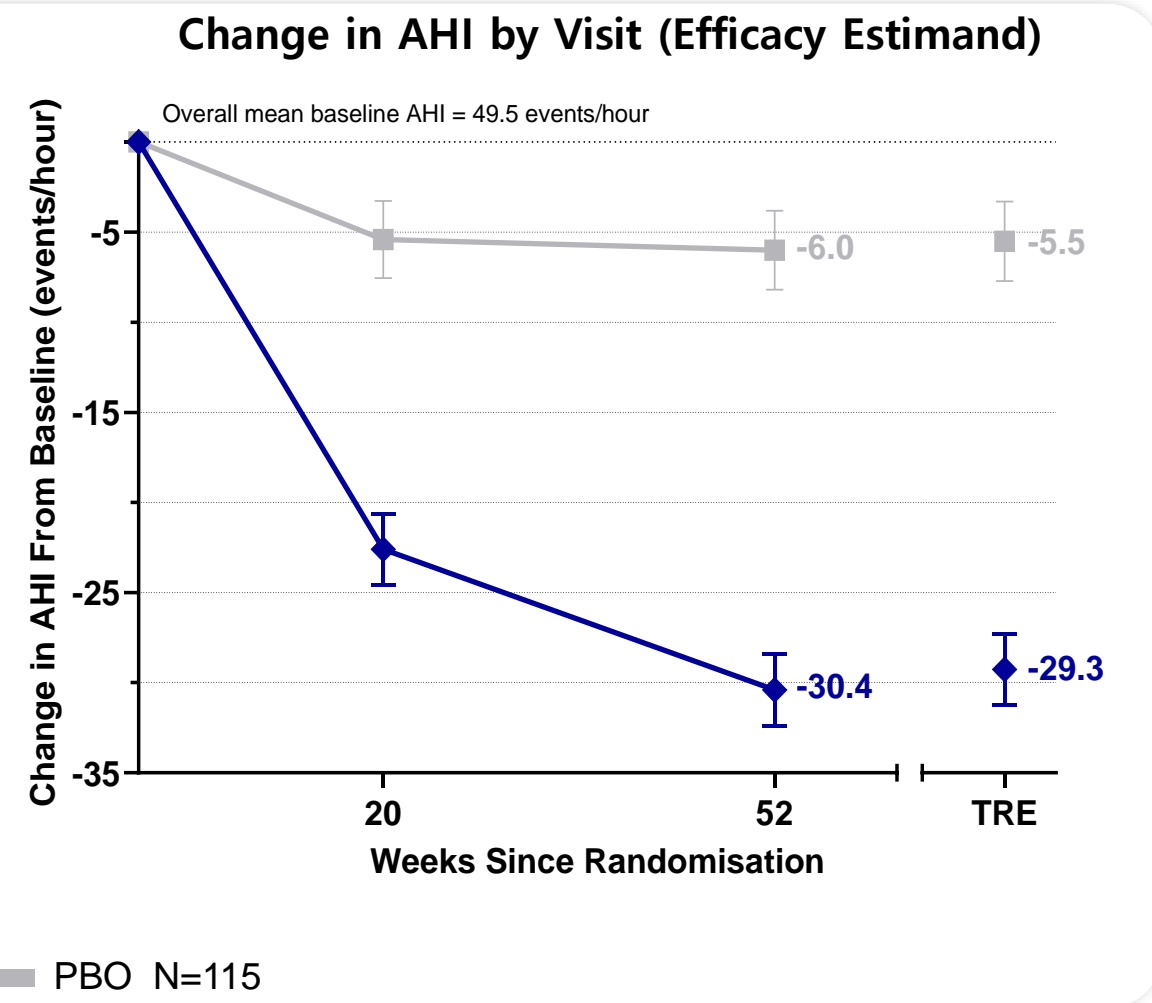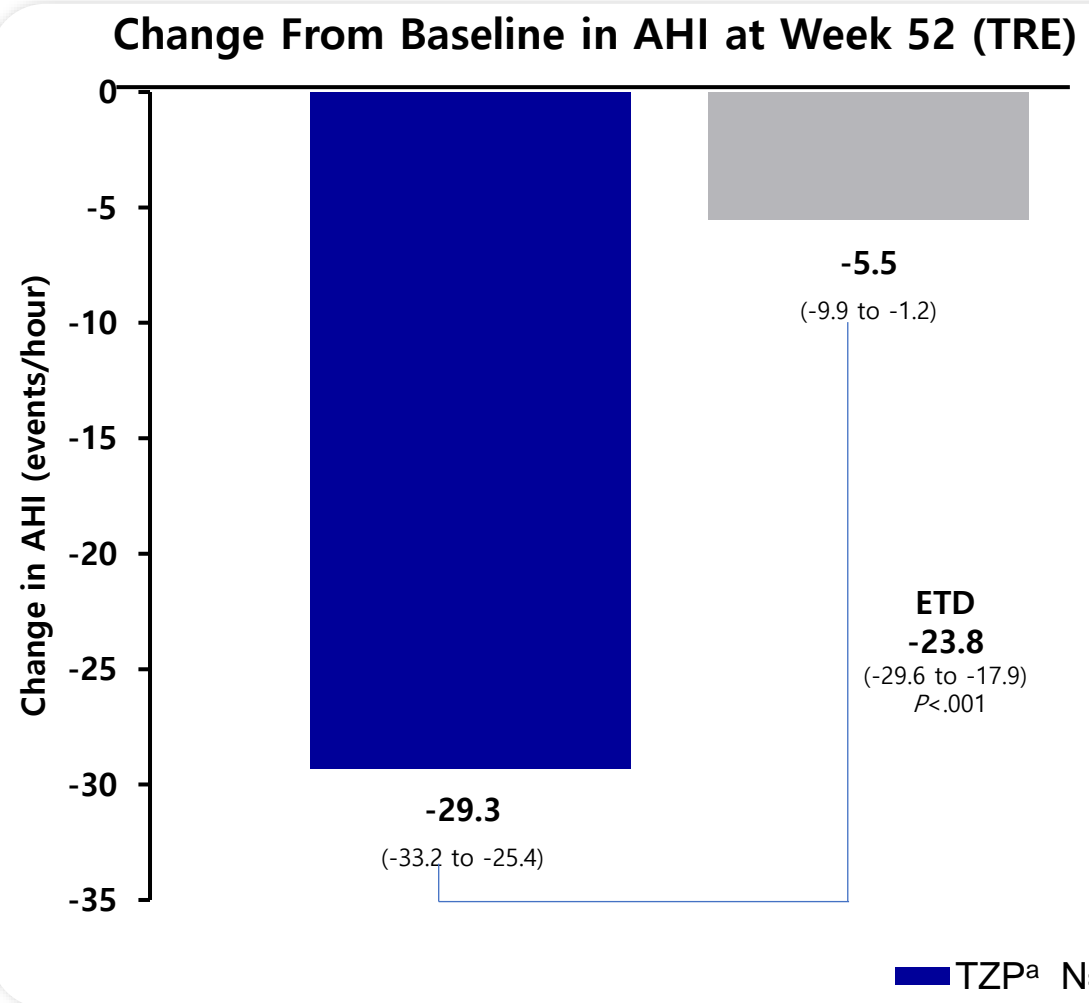| Parameters	Total (N=235)	TZP (N=120)	PBO (N=115)
AHI, events/hour	49.5 ± 26.7	46.1 ± 22.4	53.1 ± 30.2
OSA severity[b], n (%)			
No Apnoea	-	-	-
Mild (≥5 to <15 AHI events/hour)	2 (0.9)	0	2 (1.8)
Moderate (≥15 to <30 AHI events/hour)	72 (30.9)	37 (32.5)	35 (29.4)
Severe (≥30 AHI events/hour)	159 (68.2)	84 (70.6)	75 (65.8)
Missing	2	1	1
ESS	10.2 ± 4.5	10.8 ± 4.6	9.5 ± 4.4
SASHB, %min/hour[c]	137.0 (97.5)	132.2 (83.4)	142.1 (112.5)
PROMIS Sleep-Related Impairment T-Score	55.2 ± 8.9	55.3 ± 8.4	55.0 ± 9.5
PROMIS Sleep Disturbance T-Score	55.9 ± 7.6	56.0 ± 7.6	55.7 ± 7.6
Hypertension, n (%)	182 (77.4)	91 (75.8)	91 (79.1)
Systolic BP (mmHg)	130.5 (13.5)	130.5 (14.3)	130.5 (12.8)
Diastolic BP (mmHg)	81.8 (8.5)	83.2 (8.2)	80.5 (8.6)
hsCRP (mg/L)	2.8 (125.8)	3.0 (124.3)	2.7 (127.5)
HbA1c (%)	5.63 ± 0.41	5.62 ± 0.37	5.65 ± 0.44
Prediabetes n (%)	133 (56.6)	69 (57.5)	64 (55.7)
Dyslipidemia n (%)	197 (83.4)	100 (83.3)	97 (84.3)

Note: Data are mean±SD unless otherwise stated.
Footnotes, abbreviations and references are available in speaker notes section.

Change From Baseline in AHI at Week 52 (TRE)

-5.5
(-9.9 to -1.2)

**ETD
-23.8**
(-29.6 to -17.9)
P<.001

-29.3
(-33.2 to -25.4)

Change in AHI by Visit (Efficacy Estimand)

Overall mean baseline AHI = 49.5 events/hour

-6.0
-5.5
-30.4
-29.3

Change in AHI From Baseline (events/hour)

Weeks Since Randomisation

TZP[a] N=120   PBO N=115

[a]TZP MTD is a maximum tolerated dose of 10 mg or 15 mg once weekly. The starting dose of 2.5 mg TZP was increased by 2.5 mg every 4 weeks until MTD was achieved. Participants who tolerated 15 mg continued on 15 mg as their MTD. Participants who tolerated 10 mg but did not tolerate 15 mg continued on 10 mg as their MTD.
Note: Data are least-squares means (95% confidence interval) or n (%), unless otherwise stated. Changes are from baseline to Week 52.
AHI=Apnoea-Hypopnoea Index; ETD=Estimated Treatment Difference; MTD=Maximum Tolerated Dose; PAP=Positive Airway Pressure; PBO=Placebo; TRE=Treatment-Regimen Estimand; TZP=Tirzepatide.
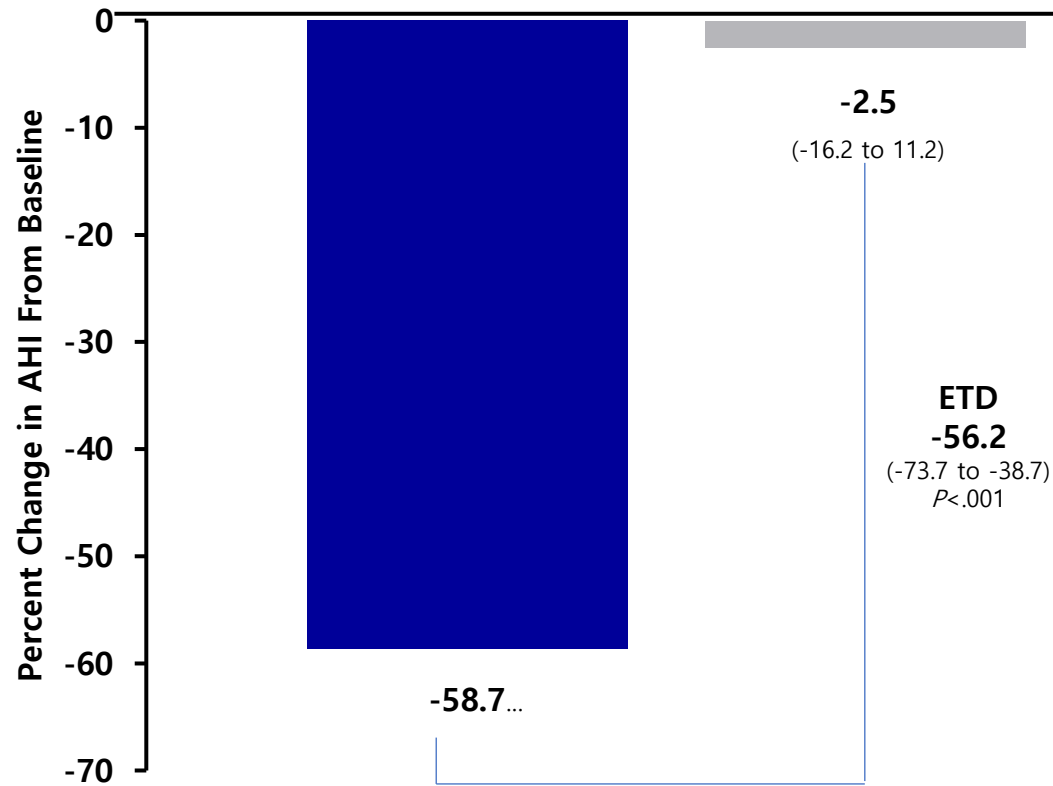Malhotra A, et al. *NEJM*. 2024;doi:10.1056/NEJMoa2404881 (Ahead of Print).   © 2024 Eli Lilly and Company

Percent Change From Baseline in AHI at Week 52 (TRE)

Percent Change in AHI From Baseline

- 0
- -10
- -20
- -30
- -40
- -50
- -60
- -70

-2.5
(-16.2 to 11.2)

ETD -56.2
(-73.7 to -38.7)
P<.001

-58.7...

Participants with AHI Reduction of ≥50% at Week 52[a] (TRE)

% Participants with AHI reduction of ≥50%

- 100
- 90
- 80
- 70
- 60
- 50
- 40
- 30
- 20
- 10
- 0

72.4%...

RR 3.1
(2.1 to 4.5)
P<.001

23.3%...

■ TZP[b] N=120   ▨ PBO N=115

Percent change in AHI at 52 weeks and participants with AHI reduction of ≥50% at 52 weeks were key secondary endpoints.
[a]RRs are calculated using g-computation methods from logistic regression. *P*-values for categorical endpoints are based on logistic regression model.
[b]TZP MTD is a maximum tolerated dose of 10 mg or 15 mg once weekly. The starting dose of 2.5 mg TZP was increased by 2.5 mg every 4 weeks until MTD was achieved. Participants who tolerated 15 mg continued on 15 mg as their MTD.
Participants who tolerated 10 mg but did not tolerate 15 mg continued on 10 mg as their MTD.
Note: Data are least-squares means (95% confidence interval) or n (%), unless otherwise stated. Changes are from baseline to Week 52.
AHI=Apnoea-Hypopnoea Index; ETD=Estimated Treatment Difference; MTD=Maximum Tolerated Dose; PAP=Positive Airway Pressure; PBO=Placebo; RR=Relative Risk; TRE=Treatment-Regimen Estimand; TZP=Tirzepatide.
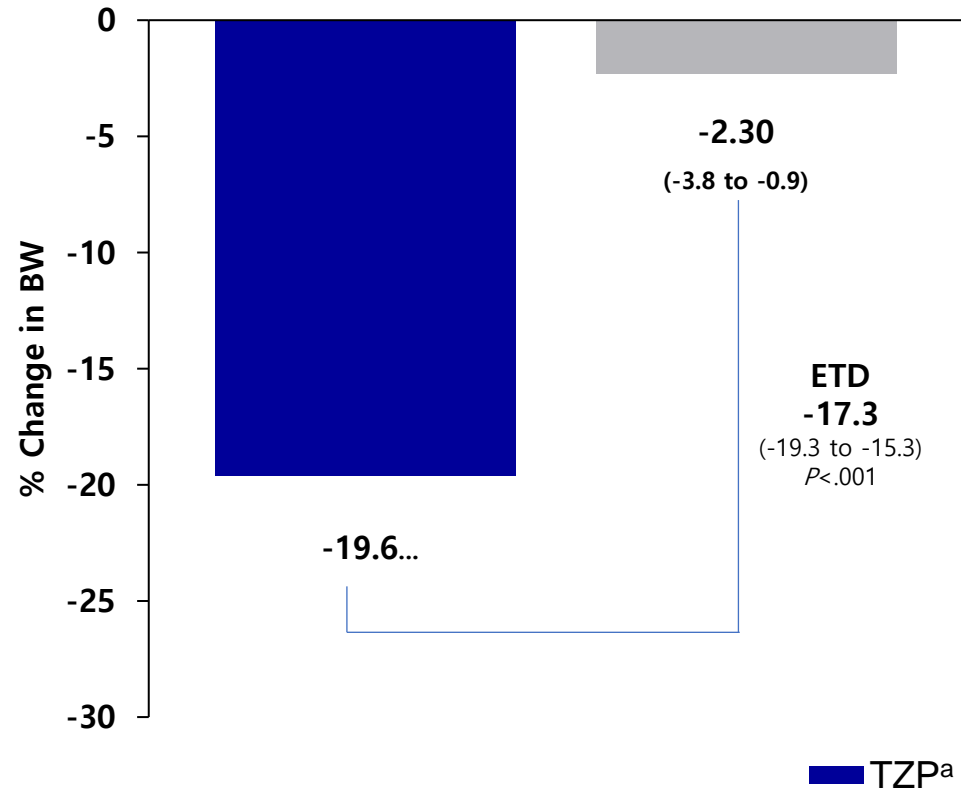Malhotra A, et al. *NEJM*. 2024;doi:10.1056/NEJMoa2404881 (Ahead of Print).   © 2024 Eli Lilly and Company
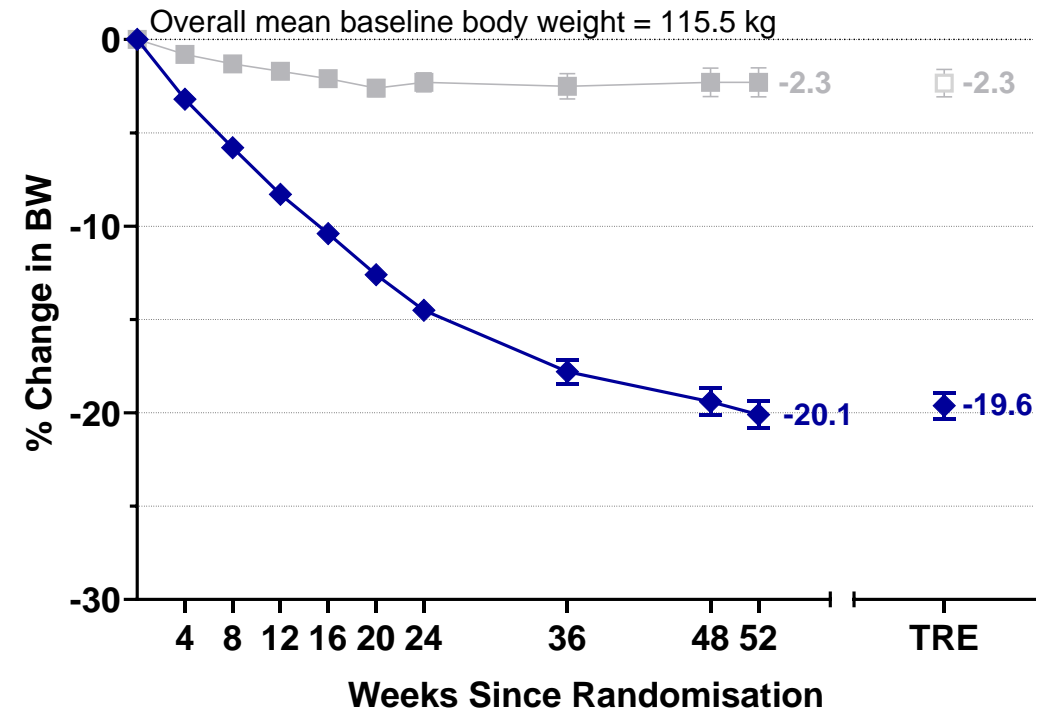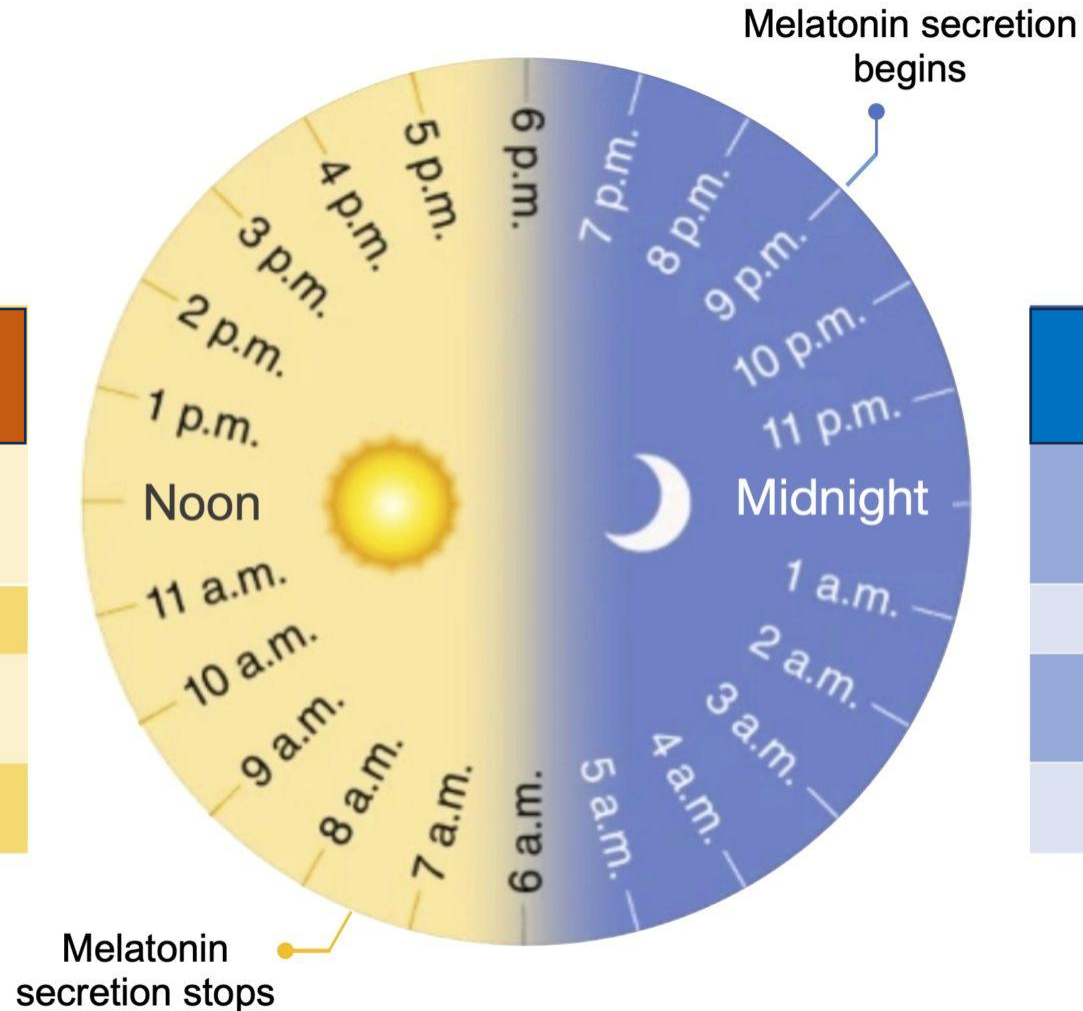
Percent Change in BW (TRE)

- -2.30 (-3.8 to -0.9)
- ETD -17.3 (-19.3 to -15.3) *P*<.001
- -19.6...

Percent Change in BW by Visit (Efficacy Estimand)

Overall mean baseline body weight = 115.5 kg

- -2.3
- -2.3
- -20.1
- -19.6

Weeks Since Randomisation: 4 8 12 16 20 24 36 48 52 TRE

TZP[a] N=120   PBO N=115

Percent change in BW at Week 52 was a key secondary endpoint.

[a]TZP MTD is a maximum tolerated dose of 10 mg or 15 mg once weekly. The starting dose of 2.5 mg TZP was increased by 2.5 mg every 4 weeks until MTD was achieved. Participants who tolerated 15 mg continued on 15 mg as their MTD. Participants who tolerated 10 mg but did not tolerate 15 mg continued on 10 mg as their MTD.

Note: Data are least-squares means (95% confidence interval) or n (%), unless otherwise stated. Changes are from baseline to Week 52.

AHI=Apnoea-Hypopnoea Index; BW=Body Weight; ETD=Estimated Treatment Difference; MTD=Maximum Tolerated Dose; PAP=Positive Airway Pressure; PBO=Placebo; TRE=Treatment-Regimen Estimand; TZP=Tirzepatide.

Malhotra A, et al. *NEJM*. 2024;doi:10.1056/NEJMoa2404881 (Ahead of Print).

일주기리듬에 따른 대사의 차이

시간제한 단식 ; 일주기리듬 단식법

- "일주기리듬단식"을 위한 이상적인 식사 시간과 단식시간
  일정

- 코티솔, 인슐린, 렙틴, 멜라토닌과 같은 신체를 활성화하고,
  수면에 영향을 주는 다양한 호르몬의 하루중 증가되고, 감소
  되는 하루 중 변화를 고려

- ➜ 잠을 자고 깨는 리듬인, **일주기리듬에 맞추어,**
- 금식하고, 식사하도록 함으로써,
- 체중도 줄이고
- 일주기리듬을 건강하게 하여
- 낮에는 더 집중도를 높이고
- 밤에는 더 좋은 잠을 자게 하는 금식법

CIRCADIAN RHYTHM FASTING

Drink only water and avoid eating at night

Avoid artificial light in the evenings

Keep the lights low at night

FAST 7PM - 7AM

EAT 7AM - 7PM

Eat breakfast early or shortly after dawn

Get sunlight exposure during the day

Plan meals at consistent, predictable times
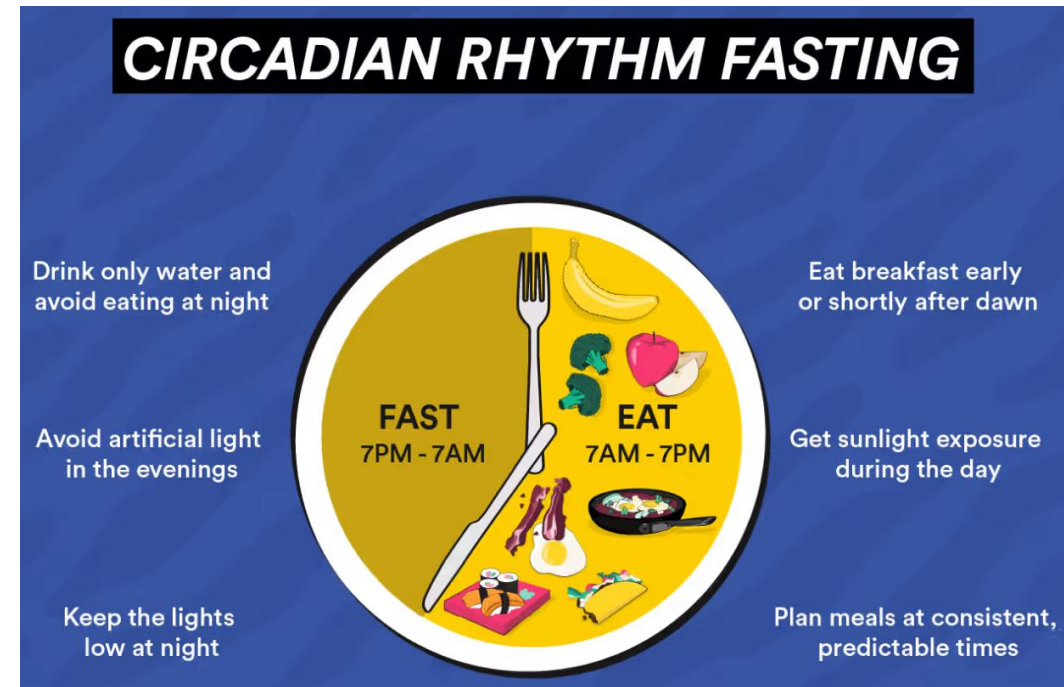
시간제한 단식법 ; 체중 감소

POPULATION
22 Men, 53 Women

Adults with type 2 diabetes and obesity
Mean age, 55 y

SETTINGS / LOCATIONS
Single academic center in Chicago, IL
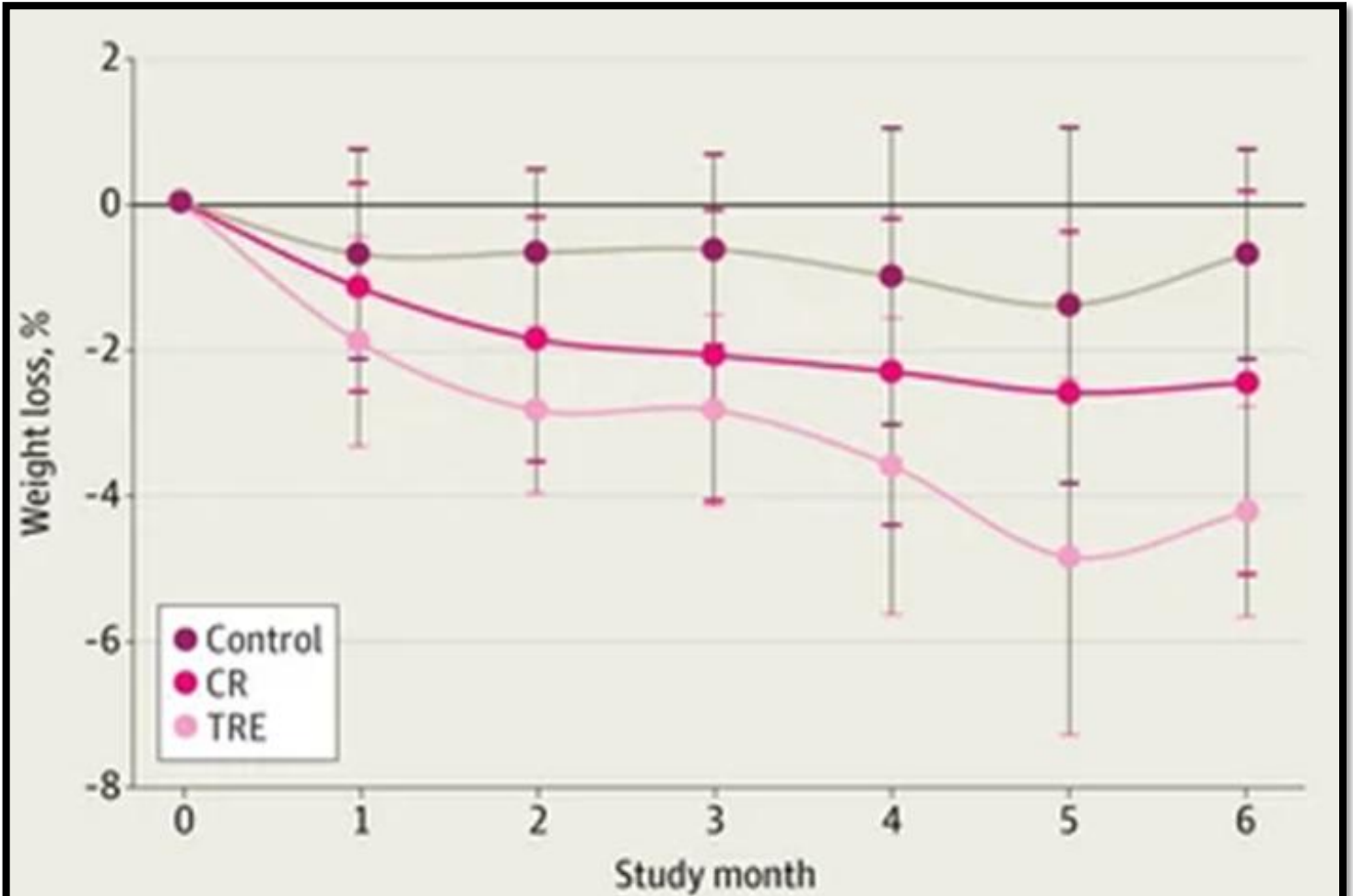
TRE group: −3.56% (95% CI, −5.92% to −1.20%); P = .004 vs control group
CR group: −1.78% (95% CI, −3.67% to 0.11%); P = .06 vs control group

일주기리듬 다이어트 잇점

1) 체중 감량

2) 체지방 감소

3) 혈압을 낮추다

4) LDL 또는 '나쁜' 콜레스테롤을 낮추고, HDL 또는 "좋은" 콜레스테롤 높인다
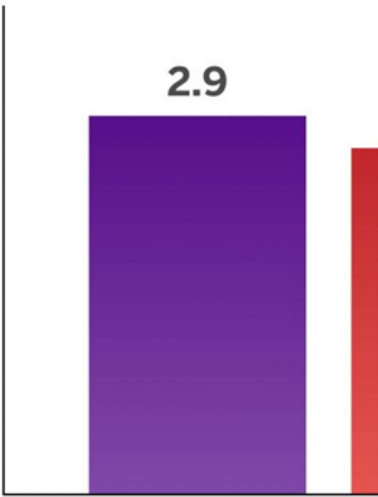
5) 공복 인슐린 수치 감소/ 공복 혈당 수치 감소/인슐린 저항성 감소

- 결과적으로 일주기리듬다이어트는,

- 당뇨병, 고혈압 및 고콜레스테롤을 예방하거나 관리

- 신체의 기능을 높이고 조절하는 일주기 리듬을 강화함으로써, 암 예방, 염증 감소, 신경퇴행성 질환 예방을 예방하고, 질병에 걸릴 위험을 낮추며, 수면 연장 효과

일주기리듬 단식법 ; 혈당, 우울증 개선
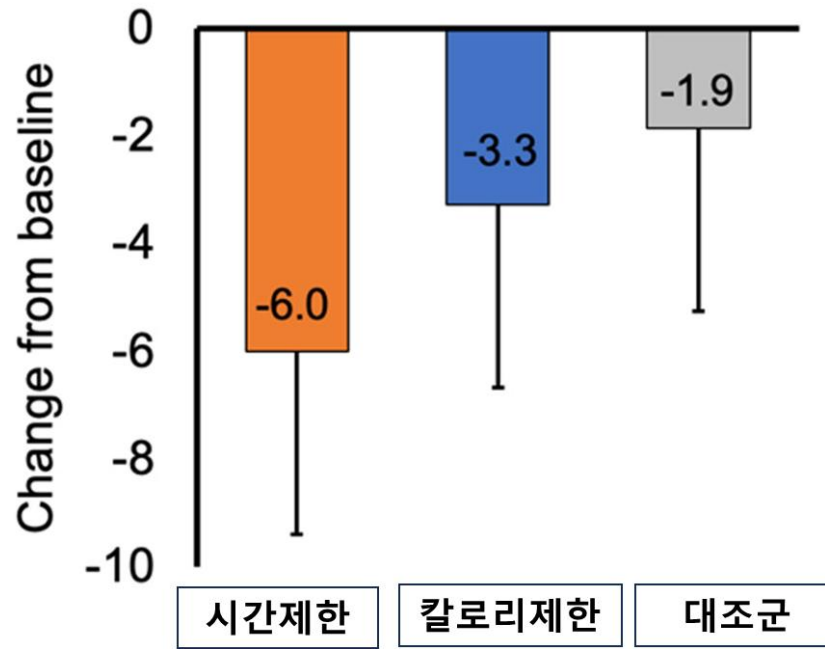
일주기리듬 단식의 효과
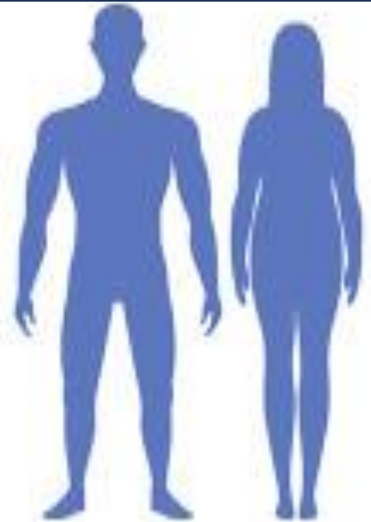
경청해주셔서 감사합니다.
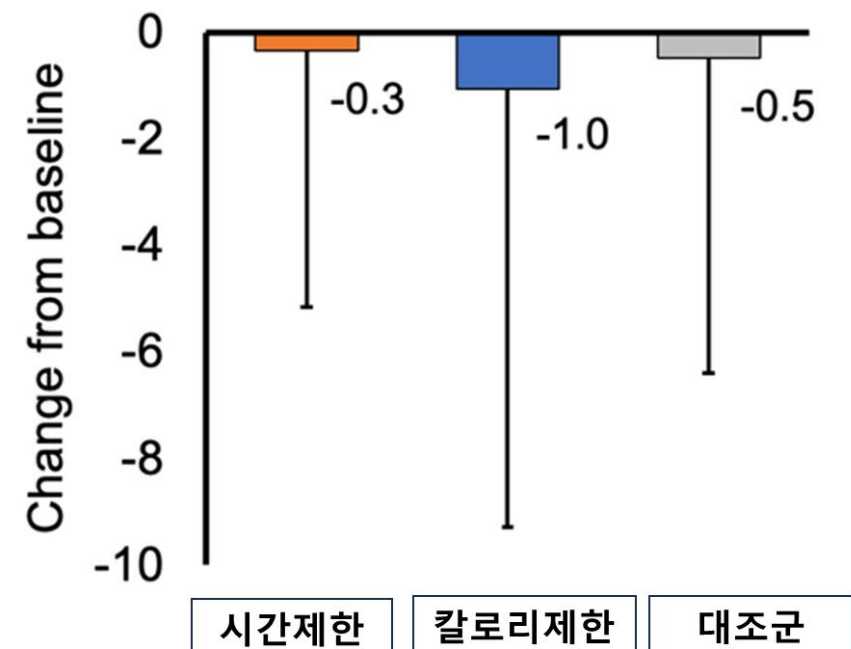
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